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LECTURES

ON

GENERAL PATHOLOGY.

A HANDBOOK FOR PRACTITIONERS AND STUDENTS.

BY

JULIUS COHNHEIM,
ORDINARY PROFESSOR OF GENERAL PATHOLOGY AND PATHOLOGICAL ANATOMY IN THE UNIVERSITY OF LEIPSIC.

TRANSLATED FROM THE SECOND GERMAN EDITION
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SECTIONS III—VI.

THE PATHOLOGY OF DIGESTION, RESPIRATION, URINARY ORGANS, AND ANIMAL HEAT.

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AUTHOR'S PREFACE TO THE FIRST EDITION.

THE appearance of this, the second volume of my lectures has been delayed—much against my wish—by my removal to Leipzig, and also by repeated and prolonged illness. I cannot, unfortunately, hide from myself that, in spite of this long delay, the book now concluded is still incomplete. An exposition of the pathology of the sense-organs and muscular movements will not be missed, for no one will have expected me to include them in these lectures; yet one section, and a most important one moreover, has been omitted,—*the pathology of the nervous system.* No one can regret this more than myself; nor have I been wanting in efforts to supply the deficiency. I have again and again applied to those who at present are regarded as the most distinguished authorities on nervous pathology in this country, in the hope that some one of them might undertake this section of my lectures; but nowhere has my request been favorably entertained. And not simply on personal grounds: I have been assured by all that a systematic exposition of the pathology of the nervous system is at the present moment impossible or at least impracticable. I am aware of course that such statements have only a relative value; yet this unanimity of the most competent judges has sufficed at any rate to deter me from attempting the thorough treatment of this portion of our science, not having at my command that most valuable aid of nervous pathology,—the regular observation of a large number of nervous cases.

Thus I have been compelled, for good or ill, to publish these lectures in their present incomplete form.

LEIPZIG; *July 20th,* 1880.

AUTHOR'S PREFACE TO THE SECOND EDITION.

In this, the second volume also, I hope that I have done justice to all the more important researches which have appeared since the publication of the first edition. Owing to the much shorter time that has elapsed, however, it has not been found necessary to make such considerable alterations as were required in the first volume.

Leipzig; *July*, 1882.

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SECTION III.

THE PATHOLOGY OF DIGESTION.

HAVING, in the foregoing section, discussed the alterations which may be produced by pathological processes in the *constitution* of the different apparatus of the human body, we are now in a position to undertake the detailed consideration of the *functional disturbances* to which the various apparatus are liable. The course to be adopted in doing so follows directly from our conception of the office of general pathology. For the *pathology of digestion, respiration,* &c., can for us have no other meaning than *the doctrine of digestion, respiration,* &c., *under morbid conditions;* under conditions, that is, *which deviate from the normal.* It will be our business, then, to analyse from this standpoint all the phases of digestion, respiration, &c., in a systematic manner; taking physiology as our model, and all the more willingly following in its footsteps as these very sections are some of the most thoroughly cultivated, and exhaustively treated, portions of the sister science. In considering the *pathology of digestion,* which will first occupy our attention, we shall, accordingly, study in succession the various divisions of the alimentary canal, and consider the several derangements to which this process is there exposed, in, and in consequence of, pathological conditions.

CHAPTER I.

THE MOUTH, PHARYNX, AND ŒSOPHAGUS.

Obstacles to mastication.—Conditions on which the secretion of saliva depends.—Salivation.—Mercurial ptyalism.—Salivation in nervous diseases.—Diminished secretion.—Buccal mucus.—Thrush.

Interference with the act of deglutition.

Narrowing of the œsophagus.—Functional disturbances of its musculature.—Spontaneous, traumatic, and secondary perforations of the œsophageal wall.—Diverticula.

Let us briefly recall the share taken by the mouth in the physiological process of digestion. Into its cavity the various substances composing our food are introduced; the fluids by being poured or sucked in, and the solids by being placed in it, or bitten off by the incisor teeth. *Mastication* then begins, and the solid pieces are divided by the incisors and crushed by the molars and premolars, as the movements made in chewing go on; while the softer portions are also bruised by the pressure of the tongue against the hard palate. During, and in furtherance of, the process of subdivision, the morsels are rolled in all directions by the tongue and by the muscles of the lips and cheeks, and at the same time intimately mixed with the fluids of the mouth. In this way the different kinds of solids are converted into a soft pulp that may be easily swallowed. This, however, is not the sole effect of the *mixed saliva,* consisting of the buccal mucus and the secretions of the salivary glands; its chemical qualities have also to be considered. For not only can the undissolved but soluble constituents of the food, such as sugar, salts, and the like, undergo solution in the mouth, but starch may there be transformed into dextrin and sugar.

You will be ready to dispense with a detailed description of the possible disturbances to which buccal digestion is exposed through the action of causes which either prevent the food from being taken into the mouth or interfere with its subdivision. I need not tell you that an individual who has lost his teeth, or fractured or dislocated his jaw, cannot bite and chew so well as another; or that a person suffering from inflammation of the tongue or other part of the mouth will be greatly inconvenienced during mastication, if only because, to avoid pain, he carefully guards against all contact with, and movement of, the tongue. The difficulty of partaking of food and chewing must be still greater in *paralysis of the muscles* of the lips, cheeks, and tongue, as well as of the muscles of mastication. Of these the m. orbicul. oris and buccinator are supplied by the facial, the tongue by the hypoglossal, and the masticatory muscles by the third division of the trigeminus. Such paralyses are sufficiently often observed, either isolated or in definite combinations; as, for example, the palsy of the lips and tongue in bulbar paralysis. When the orbicularis is completely paralysed the mouth cannot be closed. Paralysis of the muscles of mastication, if unilateral, makes chewing on the affected side impossible; if bilateral, causes the lower jaw to hang relaxed. If the tongue cannot be moved properly and with sufficient force, the food is not sufficiently subdivided and mixed with the saliva, and the patient has the greatest difficulty in converting it into a pulp that may be swallowed. A person affected with bulbar paralysis is quite commonly observed to let portions of his food fall from the imperfectly closed mouth, and to seek to assist himself in chewing by means of his fingers—an unappetising spectacle, only surpassed by the escape of particles of food and juices from the mouth through pathological apertures in the wall of the cavity. Food often so escapes in cancerous destruction of the cheek and in noma; while, in defects of the hard palate, there is danger lest it may be forced into the nasal cavity. All these conditions are so simple, and so little open to misinterpretation, that you will surely agree with me as to the expediency of turning at once to the only portion of the pathology of the mouth which demands more careful consideration, namely, alterations of the *buccal secretions*.

In pathology, just as in physiology, the constituents of the *mixed saliva* must each be attended to separately. Of one of them, the *buccal mucus*, we know, indeed, that it is the product of the entire mucous membrane of the mouth with its numerous minute mucous glands; still the conditions on which its formation depends are no better elucidated than in the case of other membranes of the same class. We are much more accurately informed with regard to the activity of the six large *salivary glands* which pour their secretions into the mouth. The most important—indeed, fundamental—fact, with which Ludwig's celebrated experiments have made us acquainted, is *the dependence of the salivary secretion on nervous influence.* During physiological life, stimulation of the salivary nerves occurs, as is known, in the great majority of instances in a reflex manner, most frequently by far through excitation of the nerves of sensation and taste of the buccal cavity. But the impulse may also be conveyed to the secretory nerves by fibres of the vagus originating in the stomach; or even by remote sensory fibres distributed to the intestines, or the genitals, or forming part of the sciatic. Moreover, the flow of saliva which accompanies mastication depends solely on the simultaneous excitation of the secretory nerves; and it is they too that convey the well-known influence exerted on the salivary secretion by certain psychical representations. After section of the salivary nerves, none of these factors can cause the flow of a single drop of saliva. On considering in addition that not only is the amount but the quality of the saliva most evidently controlled by the nervous system, it will be apparent that we have ample grounds for resorting chiefly to *nervous influences* for an explanation of any pathological alterations of the salivary secretion that may come under our notice. Nor do we meet with any serious difficulties in so doing. The fact familiar to everyone from personal experience that the presence in the mouth of a small ulcer or wound —I may remind you of the injury produced by drawing a tooth—is attended by the production of large quantities of saliva, is simply explained by the continuous irritation of the sensitive fibres of the mucous membrane. And, similarly, when certain diseases of the stomach or intestines, hysteria in many instances, and pregnancy in the first months, are associated with profuse secretion of saliva, it is the sensory nervous supply of the organ concerned that brings about the increased excitation of the salivary nerves. So long as the increase is moderate, it may, indeed, prove troublesome, and give rise to frequent spitting; still the greater part of the saliva will gradually flow unnoticed into the stomach. In the most severe cases, however, this means of escape is no longer sufficient; the saliva streams continuously out of the patient's mouth, and constitutes what is known as *ptyalism*. The latter is therefore simply the effect of an abnormally energetic and unusually persistent action of the salivary nerves; and the object of pathological analysis must be to discover in each case the cause of their abnormal excitation. Now, it is only rarely that the stimulus to true salivation proceeds from the gastro-intestinal canal or the genitals; and even ordinary inflammation of the tongue or gums is at worst associated with a more or less transitory flow. Nevertheless, it is certain that by far the most common form of ptyalism, that called forth by the *use of mercury*,[*] is a mere reflex phenomenon started in the mouth itself. True, this subject is not yet fully cleared up. A ready and rapid passage of mercury into the saliva, such as takes place with iodine or bromine, is altogether out of the question. Rather if the mercury, introduced in any way into the bodies of men and dogs, passes over at all into the pure saliva, it does so in very minute quantities,[†] and though its presence can more frequently be detected in the mixed saliva of individuals with mercurial ptyalism, the mercury may in these cases be derived from the buccal mucous membrane with its epithelial cells, of which it forms a regular tissue-constituent after its absorption into the juices of the body.[‡] Still it may be taken as most probable that it is the mercurial compounds coming into contact with the mucous membrane of the mouth that produce the general *stomatitis* which is sometimes so severe. Whether they are excreted into the mouth with the saliva or with the buccal mucus, or are introduced directly into its cavity in the form of some preparation, or as a vapour, for example, in the cure by inunction, the ensuing stomatitis brings on profuse salivation. True, the mercury, it would appear from some experiments of Von Mering* on cats, has also a directly stimulating action on the salivary nerves, and in this way augments the secretion.

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[*] Kussmaul, 'Untersuchungen über den constitutionellen Mercurialismus,' Würzburg, 1861; Bamberger, Virch. 'Hdb. d. spec. Patholog.,' vi, Abthlg. i, p. 66; Kirchgässer, 'Virch. A.,' xxxii, p. 145.

[†] O. Schmidt, 'Ein Beitrag z. Frage der Elimination des Quecksilbers aus dem Körper, mit Berücksichtigung des Speichels,' I.-D. Dorpat, 1879.

[‡] Kühne, 'Physiolog. Chemie,' p. 22.

Other cases of increased salivary secretion are not due to reflex action, though their origin is undoubtedly *nervous.* Patients with *trigeminal neuralgia* not unfrequently complain of a troublesome accumulation of saliva in the mouth, and even complete salivation has occasionally been observed in chronic cerebral diseases. The explanation of this form of salivation would not be attended by difficulty, had we always in these cases to deal with morbid processes within the cranium, the effect of which might be considered to be an abnormal and persistent *stimulation* of the facial or glosso-pharyngeal centre. Now it is true that the saliva is invariably very thin and watery, and has all the characters of the "facial secretion;" yet it hardly harmonises with such a view that the other symptoms presented by these patients point rather to a paralysis than to an excitation of the centre in question. Thus, in the progressive bulbar paralysis already mentioned, a salivation, which may sometimes be very intense, is one of the most constant symptoms, and often proves troublesome to the patient at a time when the interference with deglutition is still comparatively trifling. If, then, the ptyalism of bulbar paralysis is quite independent of the impaired power of swallowing and beyond doubt a direct result of the nervous affection, the view of Kussmaul,† who regards it as the analogue of Bernard's so-called *paralytic secretion,* would appear to have much to favour it. Nor would his view be contradicted by the fact that the salivation of these patients is considerably reduced by small doses of *atropin,* and even for a time completely arrested by this drug; for as R. Kayser‡ has shown, the same thing occurs in the paralytic secretion after division of the chorda. On the other hand, it can scarcely be reconciled with this view that the salivation in bulbar paralysis may be increased in a reflex manner, *e.g.* by galvanising the tongue;* but it is above all the quantity and long continuance (often for many months) of the flow in this disease that renders it impossible to regard it as the equivalent of the paralytic secretion of the physiologist. We must assent to the opinion of Berger† that every marked and long-continued salivation, setting in during disease of the central nervous system, should under all circumstances—even though motor paralytic phenomena are coincidently present—be referred to abnormal *stimulation* of the salivary nerve-centre; whereby it is true the different glands may be very unequally involved, even in the same individual at different periods.

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* v. Mering, 'A. f. exper. Patholog.,' xiii, p, 86.

† Kussmaul, 'Volkmann'sche Vorträge, No. 54, 1873.

‡ Kayser, 'D. A. f. klin. Med.,' xix, p. 145.

It has just been stated that salivation always supplies a secretion having the same character as that produced by stimulation of the chorda; and since the saliva produced physiologically becomes poorer in solid constituents the longer the process of secretion lasts, it must in this case also be very thin and *of slight concentration.* Its specific gravity, especially in long-continued ptyalism, may fall almost to that of water, and its contents in sugar-forming ferment be extremely low. True, the loss of ferment thus brought about will be more than counter-balanced by the quantity of saliva secreted; so that in explaining the prejudicial effects of profuse or persistent salivation on the organism, too much stress must not be laid on the imperfect transformation of amylaceous matters. Nor is the *loss of water* a factor that can throw light on the occasional striking and rapid emaciation of these patients, although in extreme cases it may amount to several litres daily, and is, as a rule, accompanied by a noticeable diminution of the urinary excretion. Much more importance undoubtedly attaches to the anorexia associated with every case of salivation, and more especially to *the great dilution and blunting of the gastric juice,* due to the constant swallowing of large quantities of alkaline saliva. To these must be added the interference with sleep, occasioned by the uninterrupted escape of the saliva, and, above all, the various pathological factors which are themselves the cause of the salivation.

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* R. Mayer, 'Virch. A.,' lxi, p. 1.

† Kayser. 'D. A. f. klin. Med.,' xix, p. 145.

Buccal digestion itself must be much more disturbed by a condition the very opposite of salivation—*i.e.* by extreme *diminution*, and, still more, by *suppression of the salivary secretion*. The latter can scarcely occur in pathological conditions, or only in such, at least, where the interference with buccal digestion is of very subordinate importance. For to complete cessation of the secretion, either the destruction of all the glands, or the absence of every nervous influence would be necessary; and though suppuration or gangrenous disintegration of the submaxillary or parotid, or occlusion of the duct by a salivary calculus or a cicatrix, followed by consecutive atrophy and wasting of the affected organ, is often observed, yet the glands still remaining, more particularly the corresponding one of the opposite side, afterwards secrete the more energetically. But the organism is fairly well protected against even a reduction of the salivary secretion by the circumstance chiefly that the production of saliva is comparatively independent of the size of the blood-stream. Arterial congestion is nothing abnormal in the secreting glands, but a strictly physiological condition; and since Heidenhain* was able to determine that the rate at which saliva is secreted is not reduced, in consequence of diminished blood-supply, until the supply of oxygen to the gland becomes inadequate, it can hardly be expected that a diminution of the secretion will result from any of the ordinary anæmias depending on disease. The same may be confidently asserted of mechanical hyperæmia, and perhaps, too, of inflammatory disturbance of the circulation. The only factor reducing the secretion, of which we have any positive knowledge, is *pyrexial rise of temperature*. This has been directly established for the parotid secretion;† and, setting analogy aside, the invariable dryness of the mouth in febrile affections renders it extremely probable that the other glands behave similarly.

When the secretion has been reduced, and the reduction is any way considerable, those phases of buccal digestion will naturally suffer most which are mainly dependent on a strong flow of water into the cavity of the mouth, viz. the conversion of the morsels into a soft pulp and deglutition. The swallowing, more especially of dry and solid food, will then be painful and extremely troublesome; since, without a plentiful admixture of liquids, the solids cannot be properly moulded in the mouth. This difficulty may be overcome by taking the greater part of the food in liquid form, or at least by sufficiently moistening the solids by drinking—a resort to which, as you know, all fever patients instinctively betake themselves. How little digestion, and the health generally, are affected by the diminution of the salivary secretion, is most strikingly proved by the state of dogs in which salivary fistulæ have been established on both sides, or from which all the glands have been removed. Fehr* observed such dogs for months together, and perceived neither wasting nor other morbid symptom; in fact, the animals behaved as usual, except that they drank more water than before the operation. Should this experiment be objected to on the ground that, the saliva of the dog containing no diastatic ferment,† it cannot fairly be applied to man, you will please remember that in human diseases the production of saliva is not completely arrested, as in these dogs, but only diminished. In fever patients, too, the power of converting starch into sugar is never absent from the saliva secreted.

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* Heidenhain, 'Studien des physiolog. Instituts zu Breslau,' iv, p. 99, 1868.

† Mosler, 'Berl. klin. Wochenschrift,' 1866, Nos. 16, 17.

That the diastatic energy of the saliva is not impaired by the presence of such foreign substances as enter the blood in any way, and then become excreted with the saliva, is still less open to doubt. The secretion of individuals who have taken preparations of iodine or bromine, though containing these elements, converts starch into dextrin and sugar no less rapidly than before. For the rest, the substances passing over from the blood into the saliva are few in number; and many very soluble bodies are not excreted through the salivary glands, even when present in considerable quantities in the circulation. The pure glandular secretion of the diabetic never contains sugar; that of the icteric never contains bile-pigment; while in the uræmic, or in animals with ligatured ureters, *urea* may with certainty be discovered in it.* A more serious, or rather the only serious, obstacle to the diastatic action of the saliva is its often observed *acidity*. When this concerns only the secretion which has become sour as the result of stagnation in the ducts, as *e.g.* the first few drops after long functional inactivity of the gland, it is quite unimportant. Still a persistent acid reaction has been seen a few times in saliva obtained from fistulæ, and the parotid secretion in particular of the diabetic, has been found by Mosler† to be sour, as a rule. On what this alteration of reaction depends is unknown. The degree of alteration will essentially determine whether the fermentative energy of the saliva so altered will be considerably reduced or not; since the transformation of amylum by the salivary diastase, while it most readily takes place in neutral or slightly alkaline solutions, is scarcely retarded by the presence of minute quantities of free acid.

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* Fehr, 'Ueber die Extirpation sämmtlicher Speicheldrüsen beim Hunde,' Inaug.-Dissert. Giessen, 1862.

† Grützner, 'Pflüg. A.' xii, p. 285.

One principal class of the causes which lead to increased secretion by the salivary glands must also augment the second constituent of the mixed saliva, that is, the *mucus*. For inflammatory irritation of the mucous membrane of the mouth, like any other catarrh, always gives rise to a more abundant production of its proper secretion. The catarrhal, is distinguished from the normal, mucus by its containing a large amount of epithelial shreds and débris, as well as by the presence in it of many lymph-corpuscles and an excess of dissolved albumen. This explains the fact that, at the commencement of mercurial ptyalism, the saliva may have a high specific gravity and be tolerably concentrated, while if the condition lasts long, the thin secretion completely gains the upper hand. Buccal digestion proper cannot, however, be interfered with by the increase of mucus, especially as its reaction continues unaltered. The rule applying to the salivary secretion holds good here also, and *a diminution must be more injurious than an increase in the production of mucus.* It is well worth noting, in this connection, that in *fever*, not only is less saliva secreted, but less mucus formed. Only in this way can we explain the tendency of the mouth of fever-patients to become dry. For Fehr found that in dogs from which all the salivary glands had been removed, there was still a sufficient quantity of alkaline liquid to keep the tongue and the rest of the mouth moist. Fever-patients, on the other hand, require for this object a regular, often repeated supply of water, failing which, the tongue acquires an intense red colour, and appears smooth and shining, as if *glazed* ; or, when the epithelium largely accumulates, becomes coated and *dry and fissured* on the surface. Hence, we do not always meet with these dry tongues in fever, even when the patient breathes through the open mouth, owing to obstruction of the nose. The mouth is parched only when he feels no thirst, or neglects to satisfy it ; in a word, when *consciousness is dulled*, and the individual is unaware of his surroundings.* It is not, you perceive, the mere question of disadvantage to buccal digestion, but much more weighty considerations that have for ages caused dryness of the mucous membrane of the mouth to be looked upon as a symptom of serious illness.

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* Kühne, 'Physiolog. Chemie,' p. 24.

† Mosler, 'Berl. klin. Wochenschrift,' 1866, Nos. 16, 17,

We have, lastly, to inquire whether, *after the secretions have accumulated* in the mouth, any factors exist, by which their activity may be impaired. Here also, from the nature of the case, the only change that can well occur is the appearance of an *intensely sour reaction* in the mouth. The condition is anything but uncommon. Not, as has been supposed, that the fluids, and in particular the mucus, ever lose their alkaline reaction spontaneously, or in consequence of inflammation ! But the mouth affords an extremely easy means of entrance for all kinds of *lowly organisms*, some of which, as you know, have the power of setting up *acid fermentations* in solutions of organic substances. I remind you of the lactic and butyric fermentations of sugar, of the acetic fermentation and the production of mould in wine ; the ferments of which decompositions have long been known to be definite, well-marked, lowly forms of fungi. These forms are universally distributed, so that the accidental presence of their germs in the mouth requires no explanation. Still their further development in healthy persons, in whom the contents of the cavity are constantly and rapidly changing, must be anything but vigorous. On the other hand, the conditions of growth are most favorable when particles of food or secretions containing epithelium are retained in the mouth, as happens in the semicomatose, in persons exhausted by prolonged suffering, or in young badly nursed and delicate children. In point of frequency of occurrence and intensity of action, by far the most important of these organisms is the *thrush fungus*, or so-called *Oidium albicans*, which had erroneously been connected with *Oidium lactis*, but was proved by Grawitz,* in an interesting communication, to be identical with *Mycoderma vini*, one of the commonest blastomycetæ. Mycoderma belongs to the great class of parasitic fungi which flourishes luxuriantly on dead organic substrata, but which can also, in exceptional circumstances, settle on uninjured tissues, and there vegetate freely. When the favorable conditions just mentioned are present, white points, the size of a pin's head, make their appearance on the inside of the lips or cheeks. These increase in number and coalesce to form delicate membranous coatings. A great part of the mouth may thus be covered, as early as the second or third day, by a material reminding one of curdled milk. This may extend low down into the pharynx, or even into the œsophagus, at first lying loosely on the surface, but adhereing rather firmly when the fungus has grown between the deeper layers of epithelium. These are the thrush-membranes which, in the new-born, are also known and dreaded under the name of "*Schwämmchen.*" They are dreaded, because their development is always accompanied by an acid fermentation of the substratum and of the fluids of the mouth; so much so that the reaction of the *saliva is markedly acid* during the entire process. The mucous membrane is considerably irritated in consequence, and children, more especially, avoid and guard against all contact with it, refusing their food. In adults, the luxuriant development of aphthæ is always a bad sign. In children, too, it proves dangerous, particularly when diarrhœa supervenes, probably as a result of the action of the fungus on the stomach and intestine, after it has been swallowed. As compared with this danger, the bad effect of the acid fermentation on the diastatic process in the mouth is quite insignificant.

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* Traube, Symptome der Krankheiten des Respirations- und Circulations-apparats,' Berlin, 1867, p. 124.

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* Grawitz, 'Virch. A.,' lxx, p. 546; lxxiii, p. 147; Rees, 'Erlanger phys.-med. Societätsber.,' Jan. 14, 1878.

From the mouth the morsels of food, saturated with saliva, are conveyed, together with the liquids, by the *act of deglutition* into the œsophagus. As you know, the tongue, pressing against the hard palate, forces the food behind the anterior pillars of the fauces, where it comes into contact with the posterior surface of the velum; and as a result the movements proper of swallowing are unfailingly initiated. Meanwhile, the anterior pillars shut off the mouth from the pharynx, by the contraction of the palato-glossal muscles. At the same time the levatores palati and palato-pharyngei draw the posterior palatine arches upwards and backwards till they touch the back of the pharynx, and so close the passage toward the posterior nares. Again, the larynx and hyoid bone being drawn upwards and forwards, the root of the tongue comes to lie over the epiglottis, which itself also closes the opening of the larynx. Thus, the only direction free for the passage of the food is toward the œsophagus, into which, as lately shown by H. Kronecker,* it is thrown by the prompt action of the musculature of the root of the tongue, aided by the striped superior constrictors of the pharynx, and is then conveyed directly into the stomach. The constituents of the food are not otherwise acted on in the pharynx; or, at most, they get an additional covering of mucus, and are thus rendered more slippery.

Apart from this last circumstance, it is evident that the performance of their function by the palate and pharynx, that is, the normal act of deglution, depends entirely on the physiological action of the muscles concerned—*provided at least that the anatomical structure of the parts is not abnormal.* I need hardly dwell on the fact that any abnormal narrowness of the passage must hinder the swallowing of the food. The narrowing may be due to cicatricial strictures, as the result, for example, of syphilis, or of poisoning by sulphuric acid; to enlargement of the tonsils, or to inflammatory swellings or tumours of the base of the skull, or of the cervical vertebræ (so-called retropharyngeal abscesses and polypi). In any case deglutition will then be impaired, and that, of course, in proportion to the amount of obstruction of the lumen of the digestive canal, which just here is at best not very considerable. On the other hand, defects or apertures in the palatine arches such as occur congenitally, or are due to syphilitic, and less often to tubercular, ulceration, must render closure towards the mouth or nose impossible, so soon at least as they reach a certain size. Liquids and small solid morsels will then pass back into the mouth, or escape into the nose during deglutition. In this respect, defects of the epiglottis are less serious; for the root of the tongue can guard the entrance to the larynx, even when the epiglottis is completely destroyed. It is also clear that deglutition must be impaired by undue sensibility of the parts, such as results more especially from acute *angina*. But it is not by pain alone that inflammations of the palate and throat interfere with swallowing; all the more severe and deep inflammations of this region, hamper rather the function of the muscles of the palate and pharynx, in consequence of the inflammatory œdema inseparable from them. A paresis of the affected muscles occurs, which in its effects, is sometimes hardly distinguishable from those of complete *paralysis*. True the action of paralysis pure and simple, may be still better observed when uncomplicated by inflammation. This is far from rare. I may remind you, for example, of the *paralysis of the palate-muscles consequent on diphtheria*, and, more important still, of *progressive bulbar paralysis*, already so often mentioned, in the clinical picture of which palsy of the muscles engaged in deglutition forms an integral part. How greatly swallowing will be interfered with in consequence of such paralyses, a moment's consideration will show. Even the first act in deglutition, the pushing of the bolus of food behind the anterior arch of the fauces, must be very imperfectly performed when the tongue is not capable of sufficently powerful movements. Fragments will remain in the different angles of the mouth, between the teeth and lips; or the patient may have to make use of his hands to push the pieces far back into the mouth. If the palate muscles are also paralysed, the active closure towards the buccal and nasal cavities cannot be effected. Fluids, more especially, will then escape into the nose, and when large draughts are taken, may also flow back through the mouth. If at the same time the constrictors of the pharynx remain unaffected, it may even happen that food and drink will be ejected with spasmodic violence from mouth and nose.* But if these muscles also are paretic, or, still more, paralytic, the greatest inconvenience, indeed danger is the result. For the morsels, having arrived in the pharynx, can get no farther, and become arrested in a dangerous region, close above the entrance to the larynx; so that whenever the patient takes food, he is alarmed by threatening suffocation, or at least runs the risk that particles may be drawn into the larynx during inspiration. The condition of such a patient is an extremely sad one, and in the end life can only be prolonged by feeding artificially by means of the œsophageal tube.

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* H. Kronecker und Falk, 'A. f. Physiolog.,' 1880, p. 296; Kronecker und Meltzer, ibid., 1881, p. 465; 'Berl. akad. Monatsber.,' Meeting of January 24th, 1881.

While in the œsophagus, the food undergoes no further chemical change; the liquids, and the morsels, rendered slippery and properly softened, are simply conveyed by the muscular contractions to the stomach. To admit of this (1) the passage must be free; (2) the muscles engaged in forwarding the food must perform their functions normally; and (3) the wall of the œsophagus must be closed in the natural way, for only then is it certain that the food will really be directed into the stomach. Accordingly, the pathological events occurring in the œsophagus can be readily determined.

The most common, and hence most important, disturbance of function, to which the œsophagus is liable, results from *obstruction of the passage* by *stenosis* of its lumen. The stenosis may be due to very different conditions. Very often it is caused by *tumours*, which compress the œsophagus *from without*; such as goitres, aneurysms, mediastinal new-growths, lymphatic glands, as well as capacious lateral *diverticula* of the gullet itself. The pressure may be confined to a limited area, or distributed over a great part of the tube. In a number of other cases, the lumen is encroached upon by *new form-*

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* Kussmaul, Volkmann'sche Vorträge, No. 54, 1873.

ations which occupy the œsophageal wall, having either originated there or involved it secondarily. Among these may be mentioned fibromas and myomas, adenomatous polypi, and —most common of all—*cancer* of the œsophagus. The *strictures* proper next claim attention. These are of two kinds: the genuine, more important variety, well termed *organic,* as, for example, the cicatricial contractions due to corrosion by sulphuric or hydrochloric acid or by caustic potash; and the spasmodic or *spastic,* which is caused by unnaturally vigorous annular contractions of the musculature—so-called *dysphagia spastica.* This form occurs most frequently in hysterical persons, but is not exactly rare as a paroxysmal affection in others. Inflammation of the gullet must also, in a sense, be regarded as an impediment to the passage of food, inasmuch as the patient dreads taking nourishment on account of the pain produced by contact with the organ. It would, indeed, play a much more important *rôle* here, were it not that inflammation of the œsophagus is uncommon, and, more especially, that the sensibility of the mucous membrane is slight. Hence this factor is completely overshadowed by the preceding ones, all of which may give rise to an extreme reduction of the lumen of the gullet.

The degree of functional disturbance caused by narrowing of the œsophagus will of course depend on the severity of the stenosis. When this is moderate, the passage of large pieces only is impeded; when very extreme, even liquids are liable to be arrested. The patient experiences the disagreeable sensation of the food sticking fast on its journey; and no matter what the actual situation of the impediment may be, it is, as a rule, referred to the region lying behind the manubrium sterni. Then he attempts to aid the passage by drinking and by swallowing other pieces; and, as a matter of fact, in less severe cases such means are usually successful in conveying the bolus of food past the narrow spot. In more severe ones, on the other hand, not only are these efforts useless, but they very often lead to a most unwished-for result—the *regurgitation* of the food into the mouth. This is not the effect of any supposititious antiperistaltic movements; it is rather due to the energetic contractions of the musculature of the œsophagus, which are excited by the voluntary efforts at swallowing. As a result, the morsels of food, being unable to pass downwards, make their escape in an upward direction; they are returned to the mouth, mixed and covered with an abundance of mucus, but otherwise unaltered. When, as is generally the case, a certain interval elapses between the swallowing of the food and its regurgitation, this depends on a gradual *dilatation* of the œsophagus, brought about by the constant accumulation of food above the constriction. The dilatation is sometimes very considerable, and with it there is usually found a *hypertrophy* of the muscular constituents of the wall. In consequence of these conditions, so little of the nourishment taken arrives in the stomach towards the termination of severe cases of stenosis—in many annular cancroids, for instance—that all possibility of feeding *per os* is at an end, and the patient literally starves. For the same reason, *congenital atresia* of the œsophagus is *eo ipso* incompatible with any length of life.

Functional incapacity of the musculature of the œsophagus, while also very fatal, is fortunately much rarer. We now know indeed from Kronecker's experiments that the peristaltic movements of these muscles play a much less important *rôle* in the ordinary act of deglutition than was formerly supposed. The swallowed morsels enter the stomach considerably before the proper peristaltic contractions of the wall of the gullet could possibly have any effect upon them. Still, in certain circumstances, if, say, the striped muscles in the region of the pharynx act too feebly or irregularly, the peristaltic action of the smooth muscles lower down may come into play, and so make it possible for the food to be administered *per os*, even in complete paralysis of the striped muscles. Again, it is obvious that the wall of the gullet (its musculature) must so behave during deglutition that no resistance worth mentioning shall oppose the passage of the food to the stomach. The canal must be open to the full; and this object is secured by nervous connections, partly of the nature of rather complicated reflex mechanisms. It has long been known that the transport of the swallowed food-pulp is greatly interfered with by destroying the innervation of the œsophagus. When a rabbit dies from the effects of the division of both vagi in the neck twenty-four hours after the operation, the gullet is found dilated and plugged with the food-pulp so characteristic in these animals. This does not, however, come from the stomach; for if no food be given to the animal after division of the nerves, the œsophagus is empty, though the stomach is, as usual, distended; and if, when dividing the vagi, you at the same time tie the œsophagus, the part below the ligature will afterwards be found free from food. As Bernard noticed, the accumulation depends rather on a tonic contraction of the lower part of the gullet, owing to which the food, instead of passing on into the stomach, becomes arrested. The condition of the cardiac end is of very special importance in the entire process. The ordinary, in a measure tonic, contraction of its musculature at once relaxes when swallowing commences, giving place to a dilatation, upon which there follows some seconds afterwards a new vigorous contraction.* It may therefore be assumed that disturbances of innervation of the cardia can essentially impede deglutition. A complete explanation of the relationship is, it is true, impossible; still we may fairly have recourse to such a view, in those cases which, though rare, have the closest resemblance to one another, and are characterised by the following features. There is an inability to completely swallow the food, and incessant vomiting, in reality, regurgitation, is complained of; yet the sound meets with little or no resistance on its passage into the stomach, while after death a more or less considerable, sometimes enormous, *fusiform dilatation* of the œsophagus is found, but no observable abnormal narrowness of the lower end of this canal.†

The third factor by which the physiological course of events in the œsophagus may be disturbed is *interruption of the continuity of the wall.* This will most often be caused by a *perforation* or a *rupture,* which may occur in an œsophagus previously sound, or in one where some morbid process or other has already prepared the way. Of the perforations involving the healthy gullet, by far the most interesting is so-called *spontaneous rupture*, which, though extremely rare, is apparently a well-authenticated occurrence. In the cases which have been accurately described, the catastrophe occurred during or immediately after a full meal, and was usually ushered in by vomiting, or at least by violent retching. An agonising pain was then felt above the region of the stomach, and was immediately followed by profound collapse. Death took place during the next twenty-four hours, the patients suffering from asphyxia of gradually increasing severity, while at the same time subcutaneous emphysema made its appearance over more or less extensive areas of the body. After the paroxysm of pain, vomiting neither took place spontaneously nor could it be artificially produced. At the autopsy, a large rent through the whole thickness of the œsophagus was always found. Its direction was usually vertical, more rarely annular, so as to completely divide the gullet transversely. The mediastinum, and sometimes the pleural cavities also, contained a large quantity of liquid, more especially any drinks taken after the catastrophe, together with an abundance of materials from the stomach. No morbid changes whatever could be discovered in the tissues bordering on the rent. These spontaneous ruptures of the œsophagus are referred by Zenker* to an *œsophago-malacia* which develops rapidly during life. He supposes that a quantity of active gastric juice is regurgitated into the gullet during the first efforts at vomiting, and that as a result of the retching, the organ itself becomes "atonic" and perhaps anæmic also. The gastric juice, being retained for a time in the gullet, causes rapid softening and thinning of the wall; so that on the next movements of deglutition or of retching a rupture occurs. Whether this explanation of the fatal event should be accepted as satisfactory, I leave to your own judgments; I cannot supply you with another. At any rate, the occurrence of such ruptures, as already mentioned, is extremely rare; and when a healthy gullet is perforated, this is caused, as a rule, by an easily recognisable trauma, such as an incised or punctured wound of the neck, or the swallowing of a sharp and angular fragment of bone. Incomparably more frequent in pathology are those interruptions of the gullet-wall which depend upon long-standing morbid processes. From without, the œsophagus may be penetrated by deep ulceration originating in the trachea, by caseated and softened bronchial glands, by aneurysms, or by cold abscesses associated with spinal caries. From within, an ulcer due to corrosion by sulphuric acid or caustic potash may in rare cases cause perforation; a result which is proportionately common when the ulceration is *cancerous*. The establishment of a perforation of the kind is under all circumstances a most dangerous event, even when antecedent inflammation has set up adhesions between the gullet and an organ in its vicinity. For ingesta can, and must, escape through the abnormal orifice into the space with which the œsophagus now communicates; and except this be the exterior, as in wounds of the neck, severe inflammation, as a rule of a gangrenous character, is wont to be excited. In cancer of the gullet more especially, some such complication usually destroys life before the stenosis has become impermeable; and, indeed, in many cancroids with a pronounced tendency to ulcerate, the signs of an abnormal communication with a neighbouring cavity may be the first thing to direct attention to the presence of a malignant tumour in the œsophagus, Rupture into the pleural or pericardial cavity is followed by a violent, often putrid, pleuritis or pericarditis; penetration of the lung, after previous adhesion, leads to gangrene of this organ; and perforation of one of the larger blood-vessels is generally attended by a rapidly fatal hæmorrhage. Most commonly, however, the abnormal communication is formed with the trachea or the right bronchus, whereupon a gangrenous broncho-pneumonia sets in, as a rule in a short time, and proves fatal to the patient.

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* H. Kronecker und Falk, 'A. f. Physiolog., 1880, p. 296; Kronecker und Meltzer, ibid, 1881, p. 465; 'Berl. Akad. Monatsber,' Meeting of January 24th, 1881.

† Cf. Zenker, Ziemssen's 'Handb.,' vii. 1; Suppl., p. 47; Strümpell, 'D. A. f. klin. Med.,' xxix, p. 211.

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* Zenker., l. c., p. 89.

While, then, in interruption of the gullet-wall as the result of perforation, the digestive disturbance proper sinks into insignificance in comparison with the other consequences to the organism, this is not so in another variety of imperfect closure of the œsophagus,—that produced by so-called *diverticula*. Two varieties may be suitably distinguished, as proposed by Zenker,*—*traction-diverticula* and *pulsion-diverticula*.

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* Ibid., p. 50, *et seq.*

The former are small, funnel-shaped protrusions of the gullet, and are distinguished by the circumstance that their pointed extremities are either involved in, or adherent to, a cicatrix. In the great majority of cases, a shrunken bronchial gland forms the point of attachment for the summit of the funnel; and since inflammation of such a gland and of the tissues surrounding it most commonly gives rise to the diverticula, the latter are mostly found at the level of the bifurcation, where the glands are most abundant. These *traction-diverticula* are far from uncommon; still, owing to their small size, they are of little importance, and the worst that can be said of them is that they may occasionally prove fatal, owing to the arrest in them of a fish-bone or other pointed object, which may cause perforation. The *pulsion-diverticula*, though incomparably less common, are therefore much more interesting. These are roundish or saccular protrusions, passing backward towards the spine or more lateral in direction, and invariably situated high up in the œsophagus, at the boundary of the pharynx. Their ætiology is less clear than is that of the traction-diverticula. When all the coats contribute to form the wall, the diverticula may perhaps be looked on as congenital; usually, however, the muscular coat is absent or imperfectly developed, and for these cases Zenker's view has much that is plausible. He conceives the earliest impulse to protrusion to consist in the impaction in the gullet of portions of solid food or of foreign bodies such as bone, or possibly in the scalding of a circumscribed area by a hot morsel —in short, in any kind of trauma. This applies only to the earliest stage of its formation; for the originally small diverticulum becomes gradually wider and deeper through distension by the food which enters it. It is this that gives it its importance and danger. Pieces passing through the gullet may miss the proper path, and enter the diverticulum through the abnormal lateral opening. These pieces may indeed be dislodged by contraction of the wall, but the expulsion is slow and irregular, so that fresh masses of food easily gain admission, and the sac may in consequence become as large as the closed hand or even as a child's head. It must then press upon the œsophagus and obstruct the entrance to it; when the usual consequences of stenosis will make their appearance, and the food *regurgitates*. But if in ordinary stenosis, with secondary dilatation above the obstruction, the taking of food is not always quickly followed by regurgitation, a still longer period is likely to elapse before the masses are expelled from the diverticulum. They are then not uncommonly already putrid, are mixed with an abundance of mucus, but always retain their alkaline reaction. In this manner, these apparently unimportant and at first insignificant structures may become so serious as to threaten life itself.*

* On the subject of this chapter, and also of the whole section, cf. the well-known text-books of special pathology by Niemeyer, Canstatt, Wunderlich, Lebert, Bamberger, and the sections dealing with digestion in Ziemssen's 'Handbuch,' &c.

CHAPTER II.

THE STOMACH.

Conditions on which physiological gastric digestion depends.—Influence of morbid processes on the secretion of gastric juice.—Disturbances of the peristaltic movements of the stomach. Interference with the action of the gastric juice.—Interference with absorption from the stomach.—Impediments to the passage of the gastric contents into the duodenum.—Frequent combination of these functional derangements.

Consequences to gastric digestion.—Dyspepsia.—Abnormal fermentations in the stomach.—Insufficiency of the stomach.—Gastrectasis.—Consequences to nutrition generally.

Vomiting.—Its experimental production.—Analysis of experiment.—Vomiting centre.—Causes capable of exciting vomiting.—Vomiting in disease of the stomach.—Vomited matters.—Importance and results of vomiting.

Solutions of continuity of the stomach.

Self-digestion of the stomach.—Ulcus simplex.—Theories concerning it.—Experiment.—Conclusions therefrom.

As regards the pathology of *gastric digestion*, to which we now turn our attention, you will not expect that it can be dealt with so briefly as was that of the mouth, &c. The much longer period spent by the food in the stomach is alone sufficient to expose gastric digestion to the attacks of various pathological processes; while the profound changes there undergone by the food make it probable *a priori* that every disturbance of the normal course of events must be of considerable importance to digestion as a whole. These events may be briefly stated to consist in the kneading of the mass of food, received from the œsophagus, by the movements of the stomach, and its intimate mixture with the secretions of the organ, especially with the *gastric juice*; the whole of the food-pulp thus acquiring an acid reaction. At the same time some soluble, but as yet undissolved, substances undergo solution, *e. g.* salts; and the saliva swallowed with the food continues its saccharifying action on the amylaceous matters, so long at least as the reaction has not become too intensely acid. Most important of all, the undissolved and insoluble albuminous bodies are converted into readily soluble and diffusible *peptones*. A portion of the materials thus rendered diffusible will then be absorbed from the stomach itself. The remainder, together with the food not yet altered by the digestive juices, is passed, a quantity at a time, through the pylorus into the duodenum, by sudden evacuations occurring at intervals. The first of these may very soon follow the entrance of food into the stomach, while the last and more copious ones do not take place till four or five hours after the meal, or even later. That these events, which together constitute gastric digestion, may occur regularly, it is obviously necessary that a normal quantity of normally constituted gastric juice should be produced, and that it should be free to act thoroughly on the ingesta. There must, moreover, be no kind of impediment to absorption or to the conveyance of the food-masses into the duodenum. These are the conditions on which gastric digestion depends, and will be our guides in the study of its pathology.

Since the *gastric juice* was first recognised, its production by the glands of the mucous membrane has always been admitted, and there could never be any doubt that processes leading to the destruction of large areas of the mucous membrane must have the effect of reducing the production of gastric juice. Similarly, the enfeebled digestion of the aged has been fairly attributed in part to senile atrophy of the gastric glands. Meanwhile, our knowledge of the finer structure of these glands, and of the events taking place in them during secretion, has so gained in breadth and precision—mainly through the researches of Heidenhain and his pupils[*]—that in judging of their morbid conditions we now feel justified, or rather compelled, to adopt more modern standards. We can no longer be content with a general statement that the mucous membrane is dull grey and the cells granular and cloudy, but demand specific details with regard to the condition of the chief and of the parietal cells, and require more especially that in estimating the appearances, due allowance shall be made for the different periods of digestion. One effect of this is to curtail very seriously the facts accumulated with reference to the pathological anatomy and histology of the gastric glands. When, *e. g.* in a gastritis, caused by alcohol, phosphorus, or other agent, the chief cells present a granular and shrunken appearance, we cannot now see in this anything but the evidence *of a continuous formation and secretion of small quantities of pepsin, without any pauses for accumulation.*[*] For this, however, the inflammatory disturbance of the circulation in the mucous membrane must be held to be at least as responsible as is the action exerted by the inflammatory irritant on the gland-cells. At any rate, the influence of other changes in the constitution and flow of the blood upon the gastric secretion has been determined with exactness. Here I place, first, the passage into the gastric juice of substances dissolved in and circulating with the blood, such as compounds of chlorine and iodine, urea, sugar, ferrocyanide of potassium, &c., some of which, like sodium chloride, decidedly promote the secretion of pepsin;[†] here, further, the fact that animals in which a hydræmic plethora has been artificially established produce large quantities of watery gastric juice; and, more important still, the fact demonstrated by Manassein,[‡] that in dogs rendered acutely *anæmic* by repeated blood-letting, the *acid* of the gastric juice is abnormally *reduced* and disproportioned to its pepsin-contents. That arterial congestion should prejudice the secretion of the

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[*] Heidenhain, 'A. f. mikrosk. Anat.,' vi, p. 368, vii, p. 239; 'Pflüg. A.,' xviii, p. 169, xix, p. 148, in Hermann's 'Handb. d. Physiol., v, 1, p. 91, *et seq.*; Ebstein, 'Arch. f. mikrosk. Anat.,' vi, p 515; Brunner und Ebstein,

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'Pflüg. Arch.,' iii, p. 565; Ebstein und Grützner, ibid., vi, p. 1, viii, p. 122; Grützner, 'Neue Untersuchungen über die Bildung und Ausscheidung des Pepsin,' 1875. Cf. also, Rollet, 'Untersuchungen aus dem Inst. f. Physiol. und Histologie in Graz.,' 1871, Hft. 2, p. 143; v. Wittich, 'Pflüg. Arch.,' v, p. 435, vii, p. 18; Friedinger, 'Wien. akad. Sitzungsber. Abth.,' iii, Bd. 71, p. 249, 1875.

[*] Ebstein, 'Virch. A.,' lv, p. 469; Grützner, 'Neue Untersuchungen,' p. 79.

[†] Grützner, l. c., p. 85; Braun, in 'Eckhard's Beiträge,' vii, p. 27.

[‡] Manassein, 'Virch. A.,' lv, p. 413.

succus gastricus is not, of course, to be expected, inasmuch as the physiological process is itself associated with such congestion. The action of mechanical hyperæmia on the secretion has not yet been investigated. As regards *inflammatory* disturbance of the circulation, the facts just quoted make it probable that it must injuriously influence the secretion of gastric juice, and with this conclusion experiment and experience are completely in accord. Beaumont had already determined on his huntsman, that every inflammatory irritation of the stomach is attended by a considerable reduction in the quantity, and lessening of energy, of the gastric juice, Since then, the opportunities presented by individuals with gastric fistulæ for carrying out exact observations under different conditions have all served to confirm the pernicious influence of gastritis on the quantity and quality of the juice secreted. One point—the *trifling amount* of the secretion—is equally dwelt on by all observers; and although the statements of writers are not quite reconcilable with regard to the pepsin- and acid-contents of the juice produced by an inflamed stomach, the explanation of this difference is probably to be found in the modus of secretion, as determined by Grützner on dogs suffering from artificial gastritis. For he found that the stomach of the dog in a condition of catarrh contrasts with the healthy organ in that it secretes *continuously*, the secretion being small in amount and not being augmented by the introduction of food into the organ. This continuously secreted juice is tenacious and cloudy, and always contains a small quantity of pepsin; on the other hand, *its reaction is far from always being acid*, but is often neutral or even alkaline—peculiarities which may partly be attributed to the simultaneous increase of mucus, depending on the catarrh. Yet it would be vain to attempt to refer all the alterations in the secretion of an inflamed stomach to the abundant production of mucus, as is clear from the closely analogous condition in acute gastritis where this element is altogether absent. Another factor should preferably be considered, one that in man at least is a very common accompaniment of somewhat severe gastritis, namely, *pyrexia*. We know that pyrexia exerts a considerable influence on the secretion of gastric juice, and tends, as a rule, *to diminish its acid con-*

tents. This result was observed by Manassein[*] on dogs, into the blood or beneath the skin of which he had injected ichorous discharges, and has repeatedly been noticed in man. Leube,[†] Kussmaul,[‡] Uffelmann,[§] and others have in fever patients examined the liquid contents of the stomach, obtained sometimes by means of the stomach-pump, sometimes as the result of vomiting, or directly from a gastric fistula, and have found that pepsin is present, generally in normal quantities, but that the acid-contents are not correspondingly large. The liquid obtained from the stomach, which was always abnormally scanty, not uncommonly gave a neutral or even alkaline reaction; and when, as in Kussmaul's[||] case, the reaction was acid, this was satisfactorily proved to depend on the presence of lactic and other organic acids, free hydrochloric acid having been altogether absent. Still, I must not conceal from you the fact that in some few cases of fever the amount of hydrochloric acid in the gastric juice has been found to be perfectly normal.[¶]

The finer mechanism, by which the secretion of the gastric glands reacts in the manner just described to circulatory disturbances and to fever, still eludes observation, and can scarcely be cleared up while the mechanism of the physiological process continues obscure. Still worse, apparently, is our prospect of obtaining an acquaintance with the action of *nervous influences* on gastric secretion; for, as you are aware, a positive demonstration of secretory nerves has not as yet been carried out in the stomach. The gastric mucous membrane, when perfectly undisturbed, does not pour out a drop of juice, while the irritation of any part of it at once sets up secretion; but should anyone therefore infer that a reflex secretory mechanism is present in the wall of the stomach itself, the objection might fairly be raised that this secretion, due to mechanical excitation, is always transitory and confined to the area stimulated, and may consequently be referred to direct stimulation of the glands. Moreover, the observations of Heidenhain* on the secretion in a portion of the fundus of a dog's stomach artificially isolated from the remainder of the organ tell rather against than for the activity of reflexly excited secretory nerves. For, though secretion took place in the isolated sac after the introduction of food *per os*, it was not till fifteen to thirty minutes had elapsed, and the amount was never considerable except when the ingesta were so easily digestible that absorption undoubtedly occurred. Even if the various statements of physiology and pathology, according to which the secretion of gastric juice is disturbed as the result of nervous excitement or shock, were more securely established than is *de facto* the case, it would still be debatable whether the movements of the stomach are not first influenced, and the process of secretion only secondarily affected. Accordingly, it is also impossible to say positively whether *a purely nervous interference with the secretion of gastric juice* really occurs; on the other hand, it can be confidently asserted that less juice will be poured out, the more feeble is the excitation of the mucous membrane by contact with its natural stimulants, the ingesta. That the nature of the food, more especially its easily digestible character or the reverse, is of consequence for the secretion has just been indicated; and the consideration of another factor, *the peristaltic movements of the stomach*, is no less important in pathology. Is it not these very movements which, in a normal condition, are of chief service in promoting the continuous and abundant separation of gastric juice during digestion, by repeatedly bringing the different portions of the mucous membrane into intimate contact with the food? Hence everything which interferes with the regularity and vigour of the peristaltic movements must prove a serious impediment to the energetic secretion of gastric juice.

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[*] Manassein, 'Virch. A.,' lv, p. 413.

[†] Leube, 'Volkmann's Vorträge,' No. 62.

[‡] R. v. d. Velden, 'Berl. klin. Wochenschr.,' 1877, No. 42.

[§] Uffelmann, 'D. A. f. klin. Med.,' xiv, p. 227, xx, p. 535.

[||] R. v. d. Velden, 'Berl. klin. Wochenschr.,' 1877, No. 42.

[¶] Uffelmann, l.c.; Sassezki, 'Petersb. med. Wochenschr.,' 1879, No. 19; Edinger, 'D. A. f. klin. Med.,' xxix, p. 555.

A more minute discussion of the causes which interfere with the *peristaltic movements of the stomach* is the more incumbent on us, as their impairment is attended by another and no less important influence on gastric digestion. We have already stated that one of the conditions of normal digestion is, that it shall be possible for the gastric juice to act thoroughly on the ingesta; and you know that this object is essentially effected by the peristaltic movements, by which the boluses of food are incessantly mixed with the juice poured out by the mucous membrane. We are not, it is true, as yet fully acquainted with the manner in which the movements of the stomach proceed under ordinary circumstances; still it is clear that they cannot take place regularly if portions of the organ are bound by firm *adhesions* to the wall of the abdomen or to the viscera, *e. g.* the liver, spleen, or pancreas. Similarly, the presence of deep cicatrices or of *cicatricial strictures* in the wall of the stomach, such as are left by an ulcus simplex, or remain after poisoning with sulphuric or hydrochloric acid, and sometimes convert the natural shape of the stomach into an *hour-glass form*, must necessarily disturb the regular course of the movements. The same may be said of tumours of the wall, whether adenomas, myomas, or carcinomas, provided they have reached a certain size. Still, you must not overestimate the evil influence of these local affections on the peristaltic movements. For the rest of the musculature can readily accommodate itself to obstacles which are confined to a limited area of the gastric wall, or can compensate their effects by correspondingly stronger contractions. A really serious interference with the peristaltic movements will rather be the result of pathological processes which involve the musculature in its entirety. In this connection should be mentioned a certain reduced irritability, or feebleness, of the muscle, or perhaps of its motor ganglion-cells, which sometimes sets in in the train of severe pyrexial diseases, *e. g.* typhoid, but is still oftener associated with general chronic anæmias. Inflammatory processes engaging the entire stomach have, further, to be taken into account, more especially the deeply seated *gastritis phlegmonosa*, but also the much commoner inflammation of the mucosa, *gastric catarrh*. In these cases, the inflammatory *œdema* of the muscularis, inseparable from every moderately intense inflammation, constitutes one source of interference with the muscular function, while another cause of muscular feebleness is the excessive and permanent stretching which accompanies the abundant production of gases in the organ, more particularly under the influence of chronic catarrh. The prejudicial effects of such distension on the functional power of the musculature of this organ more particularly, is taught by a number of other facts. I refer to the feebleness, which may go on to actual paresis, occurring in people who frequently *overload* the stomach; more especially when they make a practice of hastily swallowing large quantities of food and drink; for then the working capacity of the muscular coats almost invariably suffers, in some earlier, in others later. A gradual paresis of the musculature of the stomach will still more certainly be developed, *when the regular evacuation of the organ into the duodenum is opposed by considerable obstacles,* such as are presented by carcinomas or by fibrous strictures of the pylorus, as well as by marked narrowing of the lumen of the duodenum by cicatrices, tumours, &c. The reason that such obstacles so commonly lead in the stomach to excessive distension, and consequently to paresis of the muscle, is no doubt the peculiar manner in which the peristaltic movements take place in this organ. When the arterial ostium of one of the ventricles is narrowed, or the emptying of the bladder is interfered with by a prostatic tumour or a stricture of the urethra, the musculature of the heart or bladder, far from being paretic or even enfeebled, regularly undergoes *hypertrophy*. Notice, however, the great difference in the work done by the heart and bladder, on the one hand, and by the stomach on the other. In the two former, the *entire* muscle contracts at once, and each individual fibre produces a fraction of the movement, which is communicated to the contents of the cavity. It is not so with the stomach. The contractions of its muscular coats are peristaltic, and the transport of the ingesta from the stomach into the duodenum is in reality effected *solely by the musculature of the portio pylorica*. The strong, frequent, and unusually prolonged peristaltic movements may of course cause an increase and thickening of the musculature generally; but true and well-marked hypertrophy is usually found only in the portio pylorica, and it is not uncommon for the rest of the stomach to remain completely free from it, having been paralysed from the very first in consequence of the abnormal distension.

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* Heidenhain, 'Pflüg. Arch.,' xix, p. 148.

It is obvious that gastric digestion must suffer considerably when, owing to deficient energy of the peristaltic movements, the ingesta are not properly mixed with the gastric juice; and there are a number of other factors which may prove obstacles to the action of the gastric juice after it has been secreted. You are doubtless aware that alcohol, which in small amounts is such an efficient exciter of the gastric secretion, very seriously impairs the peptic action of the juice, when taken in large quantities and highly concentrated. Moreover, the entrance of bile into the stomach is certainly disadvantageous to gastric digestion, inasmuch as it interferes with the swelling of albuminous bodies, and may occasion the precipitation of glycocholic acid, mucus and peptones, together with which the pepsin is mechanically thrown down.[*] Indeed in those very rare cases where an abnormal communication has been formed between the gall-bladder and the stomach, in consequence of ulcerative cholecystitis, the result may, in fact, be fatal to gastric digestion. Ordinarily, however, the entrance of bile into the stomach is a transitory phenomenon, and its effect is at most a certain slowing of digestion. A much more persistent disturbance of the peptic action of the gastric juice must attend every *catarrh* of the mucous membrane. For gastritis always gives rise to more or less abundant *alkaline* transudation, and by consequence to a lessening of the acid reaction, in the absence of which peptic digestion cannot take place. If the catarrh is chronic, there is very often in addition a very considerable production of mucus, which is not only alkaline in reaction, but quite uninfluenced by the gastric juice. By this mucus the food-masses are enveloped, as though by a protecting covering, and the penetration of the gastric juice to the food is rendered difficult in consequence.

You know, moreover, that peptic digestion proceeds very slowly in a liquid which contains a considerable amount of dissolved peptone, and that the regular progress of digestion is greatly promoted by the gradual removal, during the several hours the ingesta remain in the stomach, of the peptones already formed. This object is secured, in the first place, by the *absorption* of the peptones, which normally begins in the stomach itself;[*] hence anything that interferes with absorption in the stomach must also impair gastric digestion. As regards the details of the process of absorption, and the forces co-operating therein, we are no better informed for the stomach than for the rest of the alimentary canal. Still a recent research carried out by Schmidt-Mülheim[†] in Ludwig's laboratory, has thrown light on the important share taken by the *blood-vessels* in the absorption of albuminous materials. In view of this fact, there can no longer be a doubt that every gastritis must bring about conditions unfavorable to absorption, owing to the slow movement of the blood through the inflamed mucous membrane; in saying which we for the moment leave out of account the coating of mucus on the surface of the organ, sometimes very moderate in amount. An inflamed mucous membrane continues to absorb, however; and it is possible that a severer impediment to absorption may result from somewhat considerable *mechanical hyperæmia* of the organ, such as so commonly attends cirrhosis of the liver or insufficiently compensated cardiac lesions, and then attains very marked proportions. It might be expected that the chyle-vessels would in such circumstances be available, since the flow through them may be augmented in mechanical congestion of the portal area;[‡] but it appears that absorption by their means is dependent upon the co-operation of special forces. It is, at any rate, certain that absorption from the stomach is greatly impaired when the muscular coats are functionally incapable, paretic, and the peristaltic movements feeble and confined, and we have just discussed the conditions in which this will be the case. Another portion of the peptones will be got rid of by being conveyed from the stomach into the duodenum during the periodic evacuations which commence very shortly after food is taken. In so far, therefore, as stenosis of the pylorus opposes considerable obstacles to the emptying of the stomach, it must injure digestion in the organ, and it is the more liable to do so, since under its influence a paresis of the musculature is easily developed, whereupon absorption by the stomach-wall also suffers.

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[*] Brücke, 'Wien. akad. Sitzungsber.,' 1861, Bd. xliii, p. 610; Kühne, 'Physiol. Chemie,' p. 49; Burkart, 'Pflüg. A.,' i, p. 208, ii, p. 182; Hammarsten, ibid., iii, p. 53; Schiff, ibid., iii, p. 613; Maly, in Hermann's 'Handb.,' v, 2, p. 180, *et seq.*

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[*] Cf. Tappeiner, 'Zeitsch. f. Biolog.,' xvi, p. 497; Anrep, 'A. f. Physiolog.,' 1881, p. 504.

[†] Schmidt-Mühlheim, 'A. f. Physiolog.,' 1877, p. 549.

[‡] According to unpublished experiments by Lassar in my laboratory.

The regular physiological termination of gastric digestion is *the complete emptying of the contents of the stomach into the duodenum.* The portions of food which have continued unchanged in the stomach are then handed over to the action of the digestive secretions of the intestine; and the stomach itself, being now empty, can rest and in a sense prepare itself to meet the demands of the next meal. If we ask whether pathological conditions exist, which hamper the passage of of the ingesta into the duodenum, we again meet with essentially the same familiar factors. That the transport may be effected promptly, it is above all things necessary for the door to be open; in other words, *stenosis of the pylorus,* whatever its cause, must interfere with the removal of the ingesta, and that in proportion to its severity. But since the transport of the contents of the stomach does not take place spontaneously, say, in obedience to gravity, but solely in consequence of the squeezing and pressing movements of the organ, the permeability of the pylorus is not of much value alone; the energetic action of the musculature of the stomach is also necessary. The muscular coat must be *functionally capable;* but it must also be strongly *stimulated* before energetic contractions can take place. We have, you perceive, again to deal with paresis of the gastric musculature, or rather with the group of factors which impede the peristaltic movements: and if, as is now generally believed with Brücke*, the stronger contractions at the termination of digestion are excited by the greater acidity of the juice—the acid being continuously, though probably only relatively, increased as digestion proceeds—it is obvious that the promptness and regularity of the evacuation must be impaired by all the agents formerly discussed, which lead either to the formation of a gastric juice poor in acid or to a reduction of the acidity of the juice already secreted.

It is a general characteristic of the pathology of the stomach *that one and the same factor is wont to disturb the digestive*

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* Brücke, 'Vorlesungen über Physiol.,' i, p. 312; Kretschy, 'D. A. f. klin. Med.,' xvii, p. 527.

process in many different ways. When the musculature of the organ is paretic, the normal quantity of gastric juice fails to be secreted, and the secreted juice is not properly mixed with the food; moreover, the absorption of the dissolved and diluted ingesta does not take place in a normal manner, while the transport of the contents of the stomach into the duodenum also suffers. Chronic gastritis impairs digestion by interfering with the secretion of an efficient gastric juice, by the obstacles it opposes to the action of the juice on the ingesta, and by the enfeeblement of the musculature so often setting in in its train. A carcinoma of the portio pylorica entails a diminution of the secretion owing to the loss of secretory substance; if, as so often happens, a pronounced catarrh of the stomach is developed under its influence, further injurious effects must follow: while if the tumour narrows the pylorus, the passage of the food into the duodenum will be impeded, and a secondary paresis of the muscular coat will not be long in appearing. But just because every important pathological process, when occurring in the stomach, disturbs the majority of the individual digestive acts, we are justified in at once undertaking to investigate the general question,—How under such circumstances does digestion proceed in the stomach?

The consequence of all these factors, which have just been separately discussed, is the condition known as *dyspepsia*, The term "dyspepsia" simply signifies *difficult or imperfect gastric digestion*; and that such must be the result of the action of these factors has been emphasised more than once. Whether the error consists in a deficiency or want of acidity of the juice, or in the impairment of its peptic action, owing to imperfect mixture with the ingesta, partial neutralisation of its acid, precipitation of its pepsin, or accumulation of the peptones, the inevitable effect will always be, that those substances which would normally be the subjects of gastric digestion—chiefly the albuminous bodies—are not digested in sufficient quantities. Note well what importance attaches to the circumstance just dwelt on—that in the stomach the different functional derangements have such a great tendency to become associated. For the consequence of this is the impossibility of a compensation of the error, such as we learned was so important in disease of the heart, and in other lesions of the circulatory system. If the only injurious effect of a chronic gastritis were a deficiency or want of acidity of the gastric juice, less flesh would of course be digested in the stomach, but this could be easily compensated for by the removal of a correspondingly increased amount into the intestine and its exposure to the action of the pancreatic juice. Similarly, there is apparently no reason why the prejudicial results of stenosis of the pylorus—so far at least as the digestion of albumen is concerned—should not be compensated by a proportionately abundant absorption of peptones from the stomach itself. And, on the other hand, what could be simpler than the regulation of absorption, when inadequate, by the transport of the digested food into the duodenum, where it might be taken up by the lacteals? But in reality such regulation does not, as a rule, take place. This, I need hardly say, is owing to the facts, that in an inflamed stomach not only is secretion impaired, but the peristaltic movements of the muscularis are enfeebled; that the same muscular feebleness which causes imperfect absorption is also an obstacle to the evacuation of the contents of the stomach into the duodenum; and that, on the other hand, the muscular paresis developed as the result of the stenosis makes energetic absorption impossible.

The immediate consequence, then, of the oft-mentioned functional derangements will be not simply the imperfect digestion of the food, but the *retention* of a more or less large portion of it *in the stomach, in an undigested state.* While the composition of the mass of food will depend upon the kind and composition of the nourishment taken, it usually consists of the well-known mixture of albuminous bodies, fats and carbo-hydrates, with salts and watery fluids—of substances which, with the exception of the salts, are eminently capable of *putrefaction* and *fermentation.* The non-occurrence of putrefaction in the stomach, the temperature of which is so favorable to all such processes, is, you are aware, secured in a normal condition by the acid present in the gastric juice, which gives the entire contents of the organ an intensely sour reaction. On reflecting that, in a number of the gastric lesions now under discussion, the secretion of a juice poor in acid is either the primary evil or a secondary effect, and that, in a number of others, the acid reaction is blunted, you will have no difficulty in perceiving that the immunity toward putrefactive and fermentative processes, enjoyed by the healthy stomach, must under these circumstances be seriously jeopardised. *Abnormal fermentations* in the stomach are in fact some of the most constant phenomena of dyspepsia; and it is chiefly the carbo-hydrates that fall a prey to them. The ferments necessary to their production can at all times enter the stomach, either from the mouth with the food, or from the intestine; and, so far from there being any dearth of them, it is well known that lactic acid forms almost a regular constituent of the gastric contents after carbo-hydrates have been taken. In the dyspeptic, however, not only is much more lactic acid produced than in health, but this acid undergoes further fermentation into *butyric acid, carbonic acid, and hydrogen.* Besides this butyric fermentation, in which perhaps some other members of the fatty acid series may make their appearance, *alcoholic* fermentation very commonly occurs, its final products being *acetic acid* and carbonic acid.[*] Quite peculiar fermentations may indeed be set up under these circumstances; thus Ewald[†] detected *light carburetted hydrogen* (marsh gas) in the eructations of a patient with very severe dyspepsia, while usually the gases which rise from the stomach through the œsophagus consist, you are aware, of carbonic acid and hydrogen. It is to these various and copious fermentations that the *acid pyrosis* and so-called *heart-burn* are due—symptoms often proving more troublesome to the patients than does the burdensome sensation of fulness in the epigastrium, of which, owing to the imperfect evacuation of the stomach, they usually complain. The organisms peculiar to the various fermentations are never absent from the gastric contents, in particular *yeast-cells* and all sorts of *bacteria.* Indeed, the decomposing masses of food form a very favor-

[*] Frerichs, 'Verdauung,' p. 803; Schultzen, 'Reich. u. Du Bois Arch.,' 1864, p. 491; Carius, 'Verhandl. d. naturhistor. Vereins zu Heidelberg,' iv, Nos. 6—8; 'Berl. klin. Wochenschr.,' 1874, No. 27; Budd, 'On the Organic Diseases and Functional Disorders of the Stomach,' p. 230.

[†] Ewald, 'Reich. und Du Bois' Arch.,' 1874, p. 217; 'Die Lehre von d. Verdauung,' Berlin, 1879, p. 57.

able soil for the settlement and growth of a great variety of lowly organisms, *e. g.* the delicate square packets of *Sarcinæ ventriculi*, which, as shown by Kühne,* take no part in fermentation accompanied by the development of gas.

It would be a serious error to regard the abundant production of acid in such cases as in a measure compensatory of the evil at the bottom of it—the faulty secretion in diseases of the stomach. The quantity of organic acids originating in this way—lactic, acetic, butyric—should be much greater than that of hydrochloric acid, for an efficient gastric digestion to take place; while in reality the amount produced is small, even in very severe cases. It is small, even when the patients complain of acid pyrosis and an intensely sour taste; for minute quantities of acid suffice to produce these effects, and the contents of the stomach, or the vomited matters, may have a penetrating acid odour in dyspepsia, although the amount of free acid present is not enough to intensely redden litmus-paper. These products of fermentation cannot, therefore, be of any service to gastric digestion; on the contrary, fresh disadvantages attend the fermentative processes. For the great development of gases gives rise to excessive, and especially to permanent, distension of the stomach; and if the organ was previously unable to completely meet the demands upon it, this will now be still more the case, so much so that a marked *insufficiency*† will be set up, as it has been quite properly termed by Rosenbach. That it is mainly the function of the stomach-musculature which suffers under the influence of the permanent distension, I need hardly repeat at this stage of our discussion; and it is equally unnecessary to point out what a pernicious *circulus vitiosus* is thus inaugurated for the gastric digestion of the dyspeptic.

This *circulus vitiosus* is aggravated by the fact that the products of the abnormal fermentations may act as exciters of inflammation in the stomach itself, and may thus set up gastritis or add to its severity if already present. It need excite no surprise, then, that such conditions are as a rule very obstinate, and are hardly ever perfectly recovered from, except after the adoption of a really rational line of treat[illegible] is nothing uncommon for gastric digestion in the dyspeptic to become gradually more difficult, more and more inadequate, till finally a gross change in the shape and condition of the organ, a *gastrectasis*, is the result.

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* Kühne, l. c., p. 89.

† O. Rosenbach, [illegible]

By *gastrectasis* is meant, as is well known, a dilatation of the stomach considerably in excess of the normal dimensions. Since the size of the stomach is liable to individual variations, and the organ is extremely distensible, its volume may differ greatly at different times; and it is consequently impossible to lay down absolute values, which if exceeded would necessitate our regarding the organ as ectatic or dilated: it may be very voluminous without any dilatation in a pathological sense. One is not justified in looking on the condition as morbid, *till the organ is absolutely incapable of expelling its contents in a normal manner.* Accordingly, gastrectasis is not, you perceive, so much the designation of an anatomical condition as of a functional disturbance; it involves the existence of *a permanent disproportion between* what may, in general terms, be called *the expulsive forces of the stomach, and the task which these have to accomplish.* The circumstances in which such a disproportion will arise, need not be more particularly discussed. For you know that the expulsive, evacuative forces of the stomach are simply the peristaltic contractions of its musculature, to whose share both in absorption, and in the transport of the contents of the stomach into the duodenum, we have already done full justice; and you are equally aware that their office is the propulsion of the unabsorbed contents of the stomach into the intestine, while overcoming any obstacles that may oppose this. When a disproportion arises between the two factors, either the task must be excessive, or the expulsive forces must be abnormally feeble. The former will be the case when abnormal resistances are present at the entrance to the intestine, *i. e.* in stenosis of the pylorus or compression of the first part of the duodenum, also when the stomach is excessively filled with ingesta; while the latter is evidently equivalent to a reduced functional capacity of the musculature, mus feebleness. But both conditions may coexist; and would lay special stress, more especially for ga cause abnormal resistances may be present i region, or the stomach be repeatedly overloaded, and still dilatation may for a long time fail to set in. These are the cases in which the musculature, chiefly of the portio pylorica, and to a less degree of the rest of the organ, undergoes hypertrophy in consequence of the increased call upon its work. I have already explained why such hypertrophies are neither so constant nor ever so extreme as those, for example, in the analogous lesions of the heart,—a contrast which implies that compensation, as it occurs in the stomach, can only be perfect when the lesion is moderate in degree, and must fail where the mischief is really considerable. Here then we have the second, and most important—because *per se* sufficient—condition for the origin of every gastrectasis, namely, inadequate functional capacity of the muscular coat.

These are all considerations which had to be taken into account in an exactly similar way when discussing the causes and the development of dyspepsia. In fact the differences between a dyspeptic and a dilated stomach are merely gradual; and Rosenbach* is perfectly right in regarding gastrectasis as a *progressive change*, rather than as a fully developed anatomical condition. Marked dilatation of the stomach is always preceded by the symptoms of ordinary dyspepsia, and, as already noticed, simple dyspepsia leads often enough to a true and unmistakable gastrectasis when the causes giving rise to the dyspepsia are persistent. This is easily understood. For if the dyspeptic stomach is incapable of completely evacuating its contents, and the abnormal decompositions just described distend the organ by the gases developed in their train, the food, being consequently withdrawn from the action of the muscular contractions, will tend to accumulate in the deepest portion of the organ, that is, the fundus. The latter will consequently sink towards the symphysis, and at the same time by its weight exert a continuous and not inconsiderable pull on the pylorus, whose position is much more fixed, so that the expulsion of the gastric contents will now be less easy than before. Under these circumstances, gastric digestion becomes increasingly difficult; absorption and the evacuation of the contents of the stomach into the duodenum more and more imperfect; while the decomposition and development of gases gradually increases, so that the organ in time becomes distended to such a degree as to accommodate several litres of fluid, extending with its greater curvature into the pelvis. In a stomach so dilated as this, actual digestion is reduced to a minimum. Its musculature is almost completely paretic, so that the depth of the greater curvature will be almost the same whether the organ is filled to its utmost capacity or emptied by means of the stomach-pump. The energy of the abnormal fermentations and decompositions taking place in the ectatic stomach is usually so extreme, that the patient experiences sensations as though he had at one moment a vinegar-at another a gas-manufactory in his body. The enormous production of gases leads to such considerable swelling of the stomach and prominence of the abdominal wall that a hasty inspection of such a patient makes the impression of great corpulency. But only a hasty inspection. For this apparent *embonpoint* contrasts only too sharply with the dearth of fat and flaccidity of the skin of the abdomen, and the emaciation of the remainder of the body. That emaciation is a necessary consequence of the malady now under discussion, will be evident on considering how greatly general nutrition must suffer in dyspepsia, and still more in gastrectasis. When the food lies undigested in the stomach, the body is deprived, in the first place, of all the substances which should enter it from the organ; besides the water, and the salts and other substances dissolved there, it loses the entire quantity of peptones which are absorbed therefrom. This, however, is not the only loss to the organism; the entire digestive and absorptive activity of the intestinal canal is subverted, simply because the necessary materials are not conveyed into it. When you reflect that the fats are not absorbed till they reach the intestine, and that a considerable portion of our food is rendered available for the organism only by pancreatic digestion, you will appreciate the extent of the loss accruing to the body when the chyme does not regularly pass from the stomach to the intestine. The best proof of the subversion of the function of the intestines is the invariable occurrence of *constipation* —sometimes of a most obstinate character—in persons suffering from dilatation of the stomach, while the *small quantities of urine* passed by the patients no less clearly point a considerable reduction in the amount of liquid absorbed from the digestive canal.

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* O. Rosenbach, 'Volkm. klin. Vortr.,' No. 153.

Accordingly, you cannot fail to perceive that dyspepsia in its more extreme forms, where gastrectasis and, with it, *absolute insufficiency of the stomach* have developed, is a severe disease. It is calculated not merely to destroy the subjective sensation of well-being,—a result, perhaps, partly due to a kind of self-poisoning with butyric acid, &c.*—but also to gradually undermine the entire constitution. The worst point about it is, unquestionably, that the entire process, when left to itself, becomes, in harmony with its internal conditions, a continually progressive one, for this renders the prognosis most unfavorable, unless the physician's art should avail. Indeed, it might very well excite your astonishment that individuals, the greater part of whose food remains undigested and unabsorbed in the stomach, can by any possibility live for a length of time, and do not rapidly succumb, either through inanition, or directly, through rupture of the organ. That neither the one nor the other occurs is, in fact, due to the intervention of a factor which, though not previously mentioned by us, is of supreme importance in the entire pathology of the stomach, namely, *vomiting*.

You know that by vomiting is understood the ejection of solid or liquid substances from the stomach through the œsophagus, pharynx, and mouth; and you will willingly dispense with an accurate description of the details of the act. It always commences in the same typical way with a feeling of lassitude, giddiness, and especially *nausea;* swallowing and straining movements then set in, with sweating and profuse salivation, till, after a deep inspiration, the uncontrollable *expulsion* ensues. Of all these, the final act is certainly the most important, and it must therefore be our main object to explain the mode of its occurrence. No one, who has once witnessed with what force the contents of the stomach are expelled from the mouth in vomiting, can doubt that it must be *pressure*, and very considerable pressure too, that communicates this motion to the stomach-contents. A very simple experiment serves to establish this beyond all doubt. A fasting dog is secured in a half-sitting posture on its back, and an ordinary œsophageal sound is introduced from the mouth into the stomach. The stomach is filled with a quantity of water, and the sound, protected in the usual way by a gag against the animal's teeth, is connected by an india-rubber tube with the short limb of a water-manometer. The column of water will be seen to stand just above the zero point, and alters its level a little with the movements of respiration. On subcutaneously injecting a Pravaz' syringeful of a ·2 per cent. solution of apomorphia, or introducing a few cubic centimetres of a 2 per cent. solution of tartar emetic into a superficial vein, you will notice before long, that while the dog makes the most unmistakable retching movements, and then forcibly ejects water from its mouth, the water-column of the manometer ascends very considerably, and then immediately falls to or below the zero-point. After a short pause the vomiting is repeated, and is accompanied by an almost instantaneous rise, an actual upward rush, of the water-column, followed by an equally rapid fall. This usually occurs several times before the column permanently assumes its original low level. The elevation of the water-column is very considerable, and in a strong dog may far exceed a metre.

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* Senator, 'Berl. klin. Wochenschr.,' 1868, No. 24.

What is the origin of the force, whose powerful effects you have just witnessed? The idea naturally suggesting itself is, that it is due to the very energetic contractions of the stomach. For fishes and amphibians, which do not possess a diaphragm, this is perfectly correct.* For mammals, however, the erroneousness of this idea was clearly shown by Magendie,† in a celebrated series of experiments. He ascertained, first, that when the finger is introduced into the abdomen of a dog, secured in the position already described, it is exposed during vomiting to great pressure, from above by the liver which is forced downwards by the diaphragm, and by the abdominal muscles as well as the intestines compressed by them. He determined, next, that even after extirpation of the stomach, violent retching follows the injection of tartar emetic into the veins; and, finally, he succeeded in producing vomiting of water, after the same injection, in a dog whose stomach was extirpated and replaced by a pig's bladder, filled

* Cf. Mellinger, 'Pflüg. A.,' xxiv, p. 232.

† Magendie, 'Mémoire sur le vomissement,' 1813

with water, and secured to a sound which had been introduced into the œsophagus. It was thus established that the *contractions of the diaphragm and abdominal muscles* play a very important *rôle* in the act of vomiting; still the behaviour of the stomach itself remained obscure, till fully cleared up by an excellent investigation of Rühle.* This experimenter made the stomach accessible to direct observation by a large crucial incision through the abdominal wall, and saw that with the setting in of vomiting movements, the organ, which had previously been distended by air, *rapidly collapses.* Its anterior wall approaches the posterior, and is thrown into several large folds, running down from the cardia towards the greater curvature, while the cardia itself is drawn up into the foramen œsophageum, as if into a funnel. It is—to use Traube's† expression—as though a bladder filled with air had been suddenly punctured. How independent this is of the contraction of the musculature of the stomach is most strikingly taught by a repetition of our manometer-experiment with the organ exposed—an experiment also tried by Rühle in a similar way. If we now inject the apomorphia or tartar emetic into our dog, the elevation of the water-column of the manometer is altogether absent or very trifling; sometimes, indeed, a sudden downward movement for several centimetres occurs. The experiment, when thus carried out, though convincing, is an ugly and horrible one, because the object being to produce vomiting, morphia narcosis must be avoided. It is therefore advisable to adopt a modification suggested by Gianuzzi,‡ and to carry out the experiment on a curarised dog. The dose of curare must be of such a strength that electric stimulation of the sciatic no longer leads to muscular contraction, while stimulation of the trunk of the vagus in the neck still gives rise to very evident contractions of the stomach. In a dog prepared in this way, Gianuzzi occluded the duodenum by a firm ligature, and connected the stomach with a water-manometer by means of a sound introduced into the œsophagus through an incision in the neck. When he now injected the tartar emetic into a vein, *no noticeable alteration occurred in the level of the column of water.* It may therefore be regarded as irrefutably proved that *the stomach* behaves purely passively, and *carries out no contractions during vomiting.*

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* Rühle, in Traube's 'Beiträge zur experim. Pathol.,' Hft. i, p. 1, 1846.

† Traube, 'Symptome der Krankheiten des Respirations- und Circulations-apparates,' 1867, p. 118.

‡ Gianuzzi, 'Med. Centralb.,' 1865, p. 1.

But before the stomach, when compressed by the diaphragm and abdominal muscles, can actually discharge its contents, it is necessary that no considerable resistance should oppose it; or, in other words, that an orifice, a means of exit, should be provided. Of the two natural orifices of the stomach, the pylorus need hardly be taken into account; first, because the duodenum must be exposed to the same pressure as the stomach itself, and, second, because the pylorus is usually so firmly closed that energetic contractions on the part of the musculature of the regio pylorica are required to open it. The behaviour of the cardia is the more important in the act of vomiting. We saw in the exposed stomach, that during vomiting the cardia is drawn up into the foramen œsophageum as into a funnel, and that the distended stomach collapses and falls into folds. I mentioned, too, that the pressure in the interior of the organ may fall by several centimetres water. All this would be quite unintelligible, were it not that the cardia and the gullet itself at the same time *yield and open directly.* In order to explain this yielding, various writers have assumed that an actual contraction of the longitudinal muscular coat of the œsophagus takes place. But such contraction has never been directly observed; and Lüttich* quite correctly draws attention to the fact that the character of the longitudinal fibres of the gullet in man (smooth muscle) renders a rapid, retrograde, and sudden shortening improbable. This experimenter attaches great importance to another mechanism, which, indeed, appears well calculated to thoroughly clear up the occurrence. In vomiting, whether in the dog or in man, it is not difficult to determine that the ejection of the vomited matters is preceded by a deep *movement of inspiration,* during, and subsequently to, which the glottis continues *closed.* The occurrence may be observed directly, is also testified to by the downward movement of the diaphragm, and has, moreover, been demonstrated by Lüttich by means of a tracheal manometer: its necessary consequence is a considerable *diminution of intra-thoracic pressure.* This will result in a dilatation and elevation of the gullet, and in the cessation of the entire frictional and elastic resistance which, owing to its length and narrow calibre, this canal must otherwise offer: not only so, but the evacuation of the stomach will be materially assisted by an actual suction-action of the gullet.

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* Lüttich, 'Ueber d. Mechanismus des Brechacts, insbesondere über die Betheiligung des Oesophagus,' I.-D. Kiel, 1873.

The mechanism of vomiting in man is accordingly such, that while the diaphragm and abdominal muscles contract, the gullet dilates and the cardia is opened. So energetic are the contractions that the level of the diaphragm equals that of the deepest inspiration, while the effort put forth by the abdominal muscles is not exceeded in the most forced expiration; and in this way the abdominal cavity is suddenly narrowed in all dimensions and its contents are exposed to a great increase of pressure. Since a yielding or, more correctly, open spot is present at the cardia, the material present in its neighbourhood—the contents of the stomach—will be forced through the orifice. They will be thrown into the non-resistant gullet, and now rush, often with great rapidity, into and from the mouth. Both factors, the compression of the abdomen and the dilatation of the œsophagus, are regularly combined in the act of vomiting; when one or the other is absent, actual vomiting is very exceptional. A curarised dog, with paralysed abdominal muscles, does not react to emetics by vomiting, and the greatest efforts made in straining at stool never occasion vomiting, because the cardia remains closed.

When an entire group of muscles contracts so energetically as is here the case, the cause can only be sought *in a simultaneous stimulation of the nerves supplying them.* Gianuzzi's curare-experiment also speaks very plainly for this conclusion. Moreover, another experiment, also devised by Gianuzzi,[*] has taught us, at least approximately, the situation of the centre from which the nerves concerned are stimulated. In young dogs, in which he had divided the cervical cord between the first and third vertebræ, the administration of an emetic was promptly followed by retching movements made by the muscles of the mouth and throat, while the abdominal muscles and diaphragm remained perfectly quiescent. If it follows from this that the cause exciting vomiting acts on some region of the central nervous system which is situated higher up than the spinal cord, we may fairly go a step further and seek this vomiting centre *in the group of ganglion-cells controlling the movements of respiration.* The muscles chiefly engaged in the act of vomiting, the diaphragm and abdominal muscles, are also respiratory in function; the only difference being that they are innervated alternately in respiration and simultaneously in vomiting. This agreement extends so far, indeed, that the respiratory muscles of the thorax also take part in the act of vomiting. Here, too, we have an explanation of the facts, established in Hermann's laboratory,* that emetics interfere with the production of apnœa, and strong artificial respiration with the occurrence of vomiting. True the stimulus caused by emetics is not confined to the ganglion-group of the respiratory centre: *the vomiting centre is more extensive than the respiratory.* This is proved by the swallowing and retching movements which constitute an integral part in the act of vomiting, but have nothing to do with respiration; and additional proof is afforded by certain phenomena connected with the circulatory apparatus, to which Traube† has called attention. At the commencement of vomiting, what are called *vagus-pulsations* appear in typical form; these are very large pulsations, which follow one another very slowly, and are accompanied by a *lowering of the mean arterial pressure.* With the evacuation of the stomach at the termination of the attack, on the contrary, the slowing is converted into an *acceleration of the pulse*, and the arterial pressure rises slightly above its level before the act of vomiting. The cause of these phenomena is to be sought, on the one hand, in a strong excitation of the vagus while the intrathoracic pressure is diminished, and, on the other hand, in the influence of the energetic muscular contractions on the arterial tension. That the latter does not make itself sooner felt, at the commencement of vomiting, is due to the lowering of pressure in the thorax and the stimulation of the vagus

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[*] Gianuzzi, 'Med. Centralbl.,' 1865, p. 129.

* Grimm, 'Pflug. A.,' iv, p. 205.

† Traube, l. c., p. 131.

centre by the emetic; only when these have passed off does the sudden rise of arterial pressure set in. Add to this that emetics, especially tartar emetic, which contains potash, may exert a direct pernicious action on the function of the heart. At any rate, the signs already referred to as immediately dependent on the act of vomiting warn us sufficiently to use the utmost caution in the employment of emetics with individuals who are suffering from pronounced disturbance of the circulation, more especially from heart disease.

The *causes exciting vomiting* are extremely numerous. Direct stimulation of the vomiting centre appears to be a common one; at any rate, we may thus explain the sickness of the stomach, which so frequently accompanies various diseases of the brain or its membranes, *e. g.* concussion and tumours, and which is rarely absent in basilar meningitis. A strong excitation of the expiratory centre, such as occurs in violent and prolonged fits of coughing, may extend to the entire ganglion-group of the vomiting centre proper; thus, *e. g.* the paroxysms of hooping-cough usually end in sickness of the stomach. Further, the composition of the blood, or rather the presence of certain substances in it, can stimulate the nervous centre to initiate the act of vomiting. This, in all probability, is the explanation of the tendency to vomiting observed in patients, from whose blood the excretion of essential urinary constituents is prevented, *i. e.* in the *uræmic*. That true *emetics* act directly on the centre is rendered likely by the facts of which you yourselves have been witnesses—that their injection beneath the skin or into the blood promptly gives rise to vomiting. For tartar emetic, this view has been somewhat shaken by Hermann,* whose comparative experiments showed that the salt acts much more rapidly, and in smaller doses, when introduced into the stomach than when injected into a vein. Such experiments, however, are a little deceptive, because the excitability of the vomiting centre is subject to great variations; not only different dogs, but the same animal at different times, will vomit easily or with difficulty. But Hermann succeeded in establishing another fact as the result of his experiments, namely, that when the tartar emetic is injected into the blood, the first vomit always contains antimony; and this may undoubtedly be utilised in support of his view, according to which the salt produces vomiting solely by irritation of the *peripheral* nerves, *in specie* those of the stomach. Such *indirect* excitation of the vomiting centre by irritation of some one or other centripetal nerve, is certainly by far the most general mode in which vomiting is brought about. The impulses initiating the reflex vomiting may proceed from the most different regions of the body. This form is often a very troublesome symptom of certain renal and uterine affections, and is specially prone to accompany various irritable conditions connected with the *female sexual functions;* as in pregnancy, displacements of the uterus, external adhesions of this organ, &c.; moreover, the passage of a gall-stone (*hepatic colic*) usually gives rise to obstinate sickness of the stomach. You all know with what certainty vomiting may be called forth by tickling the soft palate or touching the posterior wall of the pharynx. But in spite of all this, the most important region as regards the pathology of vomiting is the *stomach* itself; for in man and animals capable of vomiting, nothing more certainly produces sickness than irritation of the wall of the organ or of the centripetal nerves distributed through it. The nature of the irritation is comparatively immaterial, and may be of the most different kinds. Chemical means are no less potent than mechanical. If the finger be inserted through a gastric fistula into the stomach of a dog and firm pressure be made on the mucous membrane, or if a very large quantity of tepid water be introduced into the organ through an œsophageal sound, the animal immediately goes through the movements of retching, which often enough terminate in actual vomiting. The same result is equally certain, when the terminations of of the sensory nerves of the stomach are bathed in a solution of sulphate of copper or of tartar emetic. It is not surprising, therefore, that vomiting should occasionally take place in all varieties of disease of the stomach, and be very frequent in some of them. Thus, it is especially common in *ulcerative processes*, and equally so whether the ulcer is simple or cancerous; the nerves, being laid bare by the ulceration and deprived of their natural protective coverings, are more readily and strongly irritated than usual by the acid contents of the stomach. It also occurs in consequence of deep cicatrices and external adhesions of the stomach, because an abnormal dragging on the nerves will be here unavoidable. Lastly, it is met with in stenosis of the pylorus, since abnormal fulness and distension of the stomach are easily set up as the result. But such organic diseases of the stomach are not necessary to the production of vomiting; every common *dyspepsia* is calculated to bring it about, because, as already explained, it is attended by excessive distension of the organ, and, owing to the abnormal fermentative decomposition of the ingesta, by chemical irritation of the gastric nerves. Vomiting would undoubtedly be a much commoner symptom of dyspepsia, were it not that these nerves become partly habituated to the abnormal conditions, so that their excitability is gradually *blunted*. This is eminently the case in true dilatation of the stomach, when vomiting does not take place spontaneously till the organ is enormously filled with food, and the fermentations have become greatly intensified. Individuals with markedly ectatic stomachs vomit comparatively rarely and only at long intervals; and when vomiting does occur the *ejected matters are unusually abundant*. In the most advanced stages of gastrectasis, the mucous membrane may even be so insensible that spontaneous vomiting ceases to take place despite the extreme fulness of the stomach and energy of the fermentations. When emetics also fail to produce it, this is a *signum mali ominis*, because it indicates that the vomiting centre has also lost its excitability.

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* Hermann, 'Pflüg. A,' v, p. 280.

The material vomited is the *contents of the stomach*. More rarely it happens that the pylorus yields sufficiently to permit the expulsion of the contents of the duodenum, or of still lower portions of the gut, by the pressure of the abdominal muscles and diaphragm, and their ejection through the œsophagus and mouth; but this vomiting of bile, or even of fæces, is only met with when the attack is unusually violent and persistent. Even if we neglect such cases, however, the composition of the vomit varies extremely. The bulk of it usually consists of matters previously introduced into the stomach, *i. e.* the constituents of the food; but I need hardly say that products of the organism itself, which have entered the stomach, may equally well be expelled from it during vomiting. The so-called *vomitus matutinus* consists simply of saliva which has flown into the stomach in large quantities; in *hæmatemesis* we have to deal with blood which has escaped from the vessels of the stomach into its cavity; the vomit in cholera consists solely of "*rice-water*," and the occurrence of vomiting in this disease is due to the abundant secretion of this fluid from the whole digestive canal. Vomited ingesta are always mixed with the ordinary secretions of the gastric mucous membrane. Moreover, the composition of the vomit varies greatly, not only in correspondence with the nature of the food consumed, but also in proportion to the length of its sojourn in the stomach, and above all according to the functional capacity, the digestive energy, of the organ. The shorter the time elapsing between the consumption and the ejection of the food, the less will its appearance be altered. Yet when the gastric function is decidedly insufficient, portions of the ingesta may remain comparatively unchanged for hours or even days, and then be vomited, covered and saturated with tenacious mucus. But some of the constituents of the food cannot long continue unaltered. Of the carbo-hydrates I have told you, that under such circumstances they undergo extreme decomposition, and, accordingly, the vomit in dyspepsia, and still more in gastrectasis, will have a penetrating sour smell, and is often extremely offensive or even fœtid. I need not again say that yeast-cells and various schizomycetes are never absent, and that sarcinæ are also usually found in the vomited matters.

To the question, What are the *consequences of vomiting* for the organism, and *in specie* for digestion? no general reply can be given. In considering it, the act of vomiting itself may be disregarded; for the effects on the circulation have already been described, and you are yourselves aware that the violent muscular exertion often results in great exhaustion, which is by no means without its dangers for many patients. As regards digestion, the most important point undoubtedly is, that *the vomited matters are definitively withdrawn from the organism.* What this involves, you will best appreciate on considering that except for the small quantity of carbo-hydrates acted on by the saliva, the actual digestion of the food commences in the stomach. In fact, a person who habitually, during the first couple of hours after a meal, vomits everything he has eaten, will in a short time be the victim of marked inanition, and may actually die of starvation. Hence, in women who suffer during pregnancy from obstinate vomiting, uncontrollable by ordinary means, it has often been found necessary to artificially shorten the pregnancy in order to preserve life. And it is precisely the frequent vomiting that confers on many diseases of the stomach—some cases of ulcus simplex, for instance—no small degree of importance as affections attended by severe constitutional results. But vomiting is not always such a prejudicial or undesirable event. For poisonous substances which have entered the stomach may, like the ordinary constituents of the food, be removed from the organ by vomiting; and the physician often avails himself of this means to remove from the stomach matters of which it is desirable the organism should be freed. In pathology, however, more interest attaches to the fact that *the body has recourse to vomiting as a means of regulation in certain cases.* When the insufficient stomach of a dyspeptic has digested and absorbed according to its capacity, is it not really better for the patient that the useless portions of the food should be ejected, rather than remain undigested in the organ, there to undergo the abnormal decompositions already described? Such patients are unanimous in stating that vomiting always affords them considerable relief. By it the stomach is freed from a useless and injurious burden, and is thus enabled to employ its powers, however reduced, in the service of the organism at the next meal. And if additional proof of the correctness of this reasoning be required, it is afforded by the modern treatment of dyspepsia and gastrectasis, which consists, as you are aware, in the systematic evacuation of the organ by the stomach-pump—a means of securing excellent results, in a province formerly almost inaccessible to the physician's art.

It was implicitly assumed in the foregoing discussion, that the stomach forms a cavity whose parietes are *everywhere closed* except at the two orifices of the cardia and pylorus. Only in such a cavity could the chyme which is not absorbed in the stomach be secure of arriving in the intestine, the next place of digestion. It is, however, nothing rare for an *interruption* of the continuity of the wall of the stomach to take place at some spot. Leaving wounds out of account, this result is commonly due to an ulcerative process occurring in the stomach itself—a process which is most frequently cancerous, less often simple, and only rarely tuberculous or diphtheritic, and which, by gradually destroying deeper and deeper portions of the wall, finally breaks through it, giving rise to *perforation*. But the contrary may sometimes happen; and a suppurating lymphatic gland or an hepatic abscess, an ulcer of the large bile-ducts or a carcinoma of the colon, may involve the stomach and cause penetration of its cavity from without. The consequences of an opening established in any of these ways will be very different according to the size, and more especially the situation, of the aperture. Whether it is situated in the anterior or the posterior wall, in the fundus or the regio pylorica, near the greater or lesser curvature, the contents of the stomach will be pressed through it, during the peristaltic movements, in quantities, and masses, which will vary, of course, in proportion to the size of the opening. The simplest condition of affairs will be presented by an opening which leads directly outwards, *i. e.* a typical *gastric fistula*; for the loss sustained by the body through the escape of chyme may here be directly estimated, and may easily be reduced to a minimum, if not completely prevented, by artificially closing the fistula. The most pernicious results, on the contrary, attend *perforations into the cavity of the peritoneum*. For, however minute the aperture, if only the smallest quantity of fluid chyme escapes into the peritoneal cavity, a septic or purulent, and at any rate fatal, peritonitis will inevitably result. Between these two extremes are the cases of abnormal communications between the stomach and other cavities. Thus I have already (vol. iii, p. 853) described the great dangers which arise—not, it is true, to life, but to gastric digestion—from communications between the large bile-ducts and the stomach. On the other hand, if a gastric ulcer opens into the lower horizontal portion of the duodenum, as in one case observed by me, this is a comparatively harmless event; since it can make very little difference whether a portion of the chyme reaches the first part of the intestine by a byway or by the prescribed path. More important intrinsically, as well as from their greater frequency, are abnormal communications between the stomach and the colon transversum. For if the aperture is fairly capacious—and openings of 3, 4, or more cm. have repeatedly been observed—the chyme must pass in considerable quantities from the stomach into the large intestine, and in this way be practically lost to the organism. The fæces will then contain completely undigested pieces of flesh and bread, especially if the large intestine be excited to vigorous peristaltic contraction by the highly acid chyme. That such an abnormal communication between the stomach and the colon must under these circumstances prove a serious aggravation of the original disease, which, moreover, is in most cases cancerous in its nature, need not be specially dwelt on.

Before concluding our discussion of the pathology of gastric digestion, it will be well to devote a few words to a point which has excited considerable interest among physiologists, namely, the question of *the self-digestion* of the stomach. The physiologist has mainly occupied himself with an attempt to discover why it is that the organ does not during digestion digest itself; and you are doubtless aware that the alkalinity of the mucous membrane, kept up by the circulating blood, is acknowledged to be the sole factor to which the stomach owes its integrity. The correctness of this view is proved, in the first place, by the promptness with which self-digestion sets in on the cessation of the circulation after death, if an efficient gastric juice happens to be present in the organ, and if no special circumstance, such as rapid cooling of the body, interferes with the action of the juice. The product of this self-digestion is the *softening of the stomach* which was formerly the subject of much discussion, but which, since the appearance of Elsässer's* celebrated monograph, is generally admitted to be always a cadaveric change. The case of Leube,† recently brought forward as proof of the vital origin of gastromalacia, only proves, in my opinion, that a rupture of the organ had occurred *intra vitam,* and not that self-digestion had preceded death. Pathology also supplies us with a number of facts which are calculated to place in a proper light the importance of a regular circulation as the sole, and at the same time perfectly certain, means of protection against the digestive action of the gastric juice. When, as the result of corrosion or some other form of injury, or owing to ulceration, a portion of the stomach is deprived not merely of its epithelium, but of the whole depth of the mucosa as well, the naked submucosa (or muscularis) does not become digested, provided a regular blood-stream circulates through it. On the other hand, the moment the circulation of any part of the surface is interrupted, self-digestion at once commences, and spreads superficially and deeply as far as the standstill of the blood prevails. Thus every hæmorrhage into the tissues of the mucous membrane gives rise to a defect, an *erosion*. And since minute ecchymoses can make their appearance in the gastric mucous membrane in the greatest variety of circumstances, the extreme frequency of so-called *hæmorrhagic erosions* of the stomach will not appear remarkable. That tumours which have grown into the cavity of the organ escape digestion also depends solely on their vascularisation. But since the distribution of the vessels in tumours is always atypical, so that, *e. g.*, the new-formation of vessels in a carcinoma does not everywhere keep pace with the growth of its epithelium; and since, moreover, all kinds of local circulatory disturbance, bleeding, anæmia, thrombosis, &c., are of very common occurrence precisely in tumours, new growths of the stomach are very liable to undergo partial digestion. In no part of the body, in fact, do cancerous tumours ulcerate more regularly or earlier than in this organ.

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* Elsässer, 'Die Magenerweichung der Säuglinge,' 1846.

† W. Mayer, 'D. A. f. klin. Med.,' ix, p. 105.

It is certainly to digestion by the gastric juice that the "clean" base, usual in ulcers of the stomach, is due. Such ulcers are free from any covering of pus or scab, and are not coated by disintegrated, coagulated, or otherwise necrotic material. Ulcerated cancers also, as a rule, have a clean, smooth base, provided the mucous membrane which is not involved in the cancer performs its functions regularly; and when the tumour has a discoloured and ragged surface, this is invariably a sign of insufficiency of the stomach, usually dependent on chronic catarrh. The cleanness of the base of a so-called *ulcus simplex* does not, therefore, point to any conclusion with regard to its causes and mode of development; neither does the circumstance that no similar lesion is met with except in the upper part of the duodenum; for the influence of the gastric juice extends no further, being neutralised and precipitated, in short, rendered inactive, by the digestive fluids poured out into that intestine. The peculiar steep, conical shape of the ulcus simplex, corresponding as it does with the ramifications of the small arteries, might rather indicate that some pathological process in these vessels determines the development of the ulcer. But what form of circulatory disturbance could produce such results? The hypothesis of a local ischæmia due to spastic contraction of the arteries, which Klebs* regards as the starting-point of the ulcers, will hardly commend itself to you, bearing in mind the postulated duration of the arterial spasm. Virchow† inclines to the view that diseases and nutritive derangements of the vessel walls—aneurysmal or varicose dilatations, and especially obliteration and plugging—are the determining causes; and he specially emphasises the fact that the favourite seats of the corroding ulcer are the places of entrance into the stomach-wall of the branches of the coronary, gastro-epiploic, and short gastric arteries. Lastly, it has been claimed‡ that impediments to the escape of venous blood are the causal factors. Yet, however plausible these theories may appear at the first glance, and though Virchow's view more especially has met with pretty general acceptance, they are not, I am convinced, sufficient to fully elucidate the history of ulcus simplex ventriculi. And first of all, they are not borne out by pathologico-anatomical experience. Round ulcer of the stomach is distinctly a disease of early life, of that period which enjoys a marked immunity from diseases of the arteries; and only quite exceptionally have the vessels been found to be atheromatous in a stomach containing one or more simple ulcers. Again, the absence of disease of the left cardiac valves, &c., in the vast majority of such cases excludes every suspicion of embolism of a gastric branch artery. The same thing applies to mechanical hyperæmia; for while every experienced pathologist will now and then have met with cases in which the autopsy revealed cirrhosis of the liver, together with one or more unmistakable round ulcers of the stomach, it much more frequently happens that no ulceration of the stomach is found in cirrhosis of the liver, and that when ulceration is present it is not associated with obstruction of the portal circulation. Still these objections are not sufficient to overthrow the views to which they are opposed. For example, a local thrombosis of the arteries might have occurred, and yet elude observation, simply because it extended no further than the ulcer; or temporary mechanical hyperæmia, occasioned perhaps, as Key* thinks, by abnormal contractions of the gastric musculature, might have given rise first to hæmorrhage, and then to the formation of ulcers. I therefore attach more importance to experiment. It is true, for obvious reasons, that neither the ligature of single arteries of the stomach nor the occlusion of single veins will give rise to standstill of the circulation; and there will consequently be no self-digestion, and no defects as the result of such procedures. But the same object may easily be attained in another way. Panum† long ago succeeded in producing small multiple hæmorrhagic infarcts and ulcers of the stomach in dogs, by injecting an emulsion of wax through a long catheter introduced into the central end of the femoral artery; still his animals died, owing to the great number and wide distribution of the emboli, and as death occurred mostly within twenty-four hours after the injection, the time was not sufficient to allow of any conclusion as to the fate of the ulcers so produced. Some years ago I adopted a modification of this experiment: the stomach was exposed, and the injection, consisting of chromate of lead in suspension, was thrown directly into one of the gastric branches of the splenic artery, instead of into the femoral and aorta. By inserting the cannula pretty deeply, I could generally succeed in completely occluding the branches entering the submucosa and mucosa, the muscular twigs remaining almost free. The result was that all the animals which died or were killed on the next and following days presented *large ulcers with precipitous walls and perfectly clean bases*, as a rule of long elliptical form; moreover, the detection of the chromate in the larger branches leading to the ulcers was extremely easy. In the animals which lived till the end of the second week, instead of one large ulcer, several small defects were usually found; and after the termination of the third week I invariably saw, not an ulcer, but a *perfectly smooth undamaged mucous membrane*, while the ligature and the presence of chromate of lead in a few arterial branches allowed no doubt as to the locality of the previous occlusion: in short, the ulcer had completely healed. Corresponding results have been obtained by myself and by several other experimenters* after injuring the stomach by corrosion, burning, bruising, or wounding: all losses of substance so produced healed, during the course of a few weeks, when the dogs or rabbits remained alive. In human beings, also, several cases are on record where the mucous membrane has been caught and torn away by a sound introduced into the stomach, and where, nevertheless, the membrane was discovered at the post-mortem to be perfectly smooth and intact.†

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* Klebs, 'Handb. d. pathol. Anat.,' p. 185.

† Virchow, his 'A.,' v, p. 362.

‡ Günsburg, 'A. f. physiol. Heilkd.,' xi, p. 521; A. Key, 'Hygeia,' 1870, p. 261, ref. in 'Virchow-Hirsch's Jahresber.,' v, 1870, ii, p. 155.

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* A. Key, 'Hygeia,' 1870, p. 261.

† Panum, 'Virch. A.,' xxv, p. 488.

You now perceive the real difficulty in understanding the simple ulcer of the stomach. It is not so much its mode of origin that requires explanation as the circumstance that *it usually so obstinately refuses to heal.* Not that an ulcus simplex cannot heal. The sufferings occasioned by such an ulcer finally disappear in many cases, and the pathological anatomist almost daily meets with cicatrices of the stomach which are nothing but the remains of a healed ulcus rotundum. But if these ulcers can heal, why, we may fairly ask ourselves, do months and years elapse, as a rule, *without the occurrence of healing?* It must honestly be confessed that our knowledge of ulcus simplex is very fragmentary. We are ignorant whether it originates rapidly or gradually, and while it is certain that it may grow larger and more especially deeper, and is justly termed *corroding* or *perforating*, we do not know whether its growth takes place slowly and continuously, or only at intervals. One thing is proved by innumerable clinical observations—that the malady is an exquisitely *chronic* one. And if this fact be taken in conjunction with the experimental results just described, you will readily admit that the theories which seek the origin of the round ulcer of the stomach in certain circulatory disturbances do not fully meet the case. In the stomach of such patients there must be present in addition an unknown something *which prevents the healing of the ulcer*. But whether, as has more than once been suggested, this something consists in an abnormal acidity of the gastric juice, we have as yet no positive investigations to show. Quincke* is besides of opinion that a general anæmia may act in this direction.†

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* Quincke, 'Correspondenzbl. d. Schweizer Aerzte,' 1875, No. 4; 'Mittheilungen des Vereins Schleswig-Holsteiner Aerzte,' Heft 9, No. 2. W. Körte, 'Beitrag z. Lehre vom rund. Magengeschw.,' Inaug.-Dissert., Strassburg, 1875.

† W. Leube, 'D. A. f. klin. Med.,' xviii, p. 496; cf. also Hänisch, ibid., xxiii, p. 579.

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* Quincke, 'Correspondenzbl. d. Schweizer Aerzte,' 1875, No. 4; &c.

† On the subject of this chapter consult, in addition to the handbooks mentioned in foot-note, vol. iii, p. 844, Beaumont, 'Experiments and Observations on the Gastric Juice and the Physiology of Digestion,' 1874; Frerichs, in R. Wagner's 'Handb.,' Bd. iii, 1, art. "Verdauung," 1846; Schiff, 'Leçons sur la Physiologie de la Digestion,' 1865; F. W. Pavy, 'A Treatise on the Function of Digestion; its Disorders and their Treatment,' 1869.

CHAPTER III.

THE LIVER.

Peculiar position of the liver in the circulation.—Slowness of its blood-stream.—Importance of hepatic affections as influencing the constitution of the blood.

Behaviour and conditions of the physiological secretion of bile.—Pathology of the biliary secretion.—Influence of circulatory disturbances, of alterations in the constitution of the blood, and of fever upon the biliary secretion.—The secretion of bile in destruction and morbid states of the hepatic cells.—Polycholia and acholia.

Physiology of the excretion of bile.—Inaccessibility of the gall-bladder.—Hydrops cystidis felleæ.—Stagnation of bile.—Gall-stones.—Their formation.—Pathological apertures in the bile-passages.—Abnormal communications between the bile-passages and other cavities.

Obstruction of the bile-passages.—Icterus catarrhalis.—Icterus neonatorum.—Action of the bile in the intestine.—Effects of a deficiency of bile on digestion.—Influence of occlusion of the bile-ducts on the formation of bile.—Absorption of the stagnant bile.—Icterus.—Excretion of the bile-pigment by the kidneys.—Absorption and abode of the cholates.—Icterus gravis.—Cholæmia.—Acute atrophy of the liver.

Physiology of the hepatic glycogen.—Its relation to the sugar of the blood.—Artificial diabetes mellitus.—Methods.—Its relation to the liver.—Critique of Bernard's theory. Wide distribution of glycogen in the body.—Pathological diabetes mellitus.—The richness of the blood in sugar forms the central point of all the symptoms.—Mild and severe forms of diabetes.—Pathological anatomy of diabetes.—Albuminous waste and decomposition of sugar in the diabetic.—Muscle-diabetes.

When the food-pulp has passed the pylorus, it is at once exposed to the action of a number of new digestive juices, some of which are produced by the intestine itself, while others, secreted by glands lying outside the gut—the liver and pancreas—are poured into its lumen. As the secretions of these glands become mixed with the chyme in the first portion of the intestine, or duodenum, we may suitably commence the pathology of intestinal digestion by considering them, and shall take first the *liver*, with its secretion, *the bile*.

A real *pathology of the liver*, a discussion, that is, of the manner in which the organ performs its functions under abnormal conditions, is still, indeed, a desideratum, for the simple reason that the physiology of the liver has not yet been sufficiently worked out. Of what service would it be to enumerate all the functions and derangements of function which have been ascribed by the pathologists of former centuries to this their favourite organ? The little positive knowledge we have of the *rôle* entrusted to the liver in the economy of the organism does not, in my opinion, admit of our drawing far-reaching conclusions as to its pathology. So far as I see, the following are the points which chiefly concern us. In the first place, the *relationship of the liver to the circulation* is quite peculiar, and differs from that of every other organ, inasmuch as while they are only supplied by one or several branches from the aortic system, it receives by far the greater part of its blood from the portal vein. The consequence of this is that every kind of circulatory disturbance of the liver must react very readily and markedly on the blood-stream in the venous tributaries which by their union form the vena portæ, the veins, *i.e.*, of the spleen, pancreas, stomach, and entire intestinal canal, except the rectum. It is more particularly the *increase of resistance* in the area of the portal and its branches that, if marked and uncompensated by a collateral circulation, invariably leads to engorgement of the vessels of the organs just named, with its attendant consequences. But although these stagnations form a constant and highly important feature in the clinical picture of hepatic cirrhosis, pylethrombosis, and tumours situated in the neighbourhood of the portal fissure, we shall not now dwell upon them, since we have already dealt with the relations involved, Ascites as the result of stagnation is to you a familiar phenomenon; and when, in any of the foregoing diseases, the venous tributaries of the portal are tensely filled and distended, while the implicated organs are the subjects of marked mechanical hyperæmia, and numerous capillary, or even larger, hæmorrhages take place into and from the mucous membrane of the alimentary canal, all these effects are in entire conformity with the results which you know attend mechanical hyperæmia. On the other hand, you will remember that it was the vena portæ I selected with a view to demonstrate what important consequences may result from the accumulation of the blood in a venous territory to the circulation beyond the obstruction, and in this instance, indeed, to the entire circulation of the body. Complete and sudden occlusion of the portal vein causes death in rabbits, and in dogs gives rise at least to a considerable fall of arterial pressure. And when, as usually happens in human pathology, the occlusion is gradual in its development, it will be the completeness or incompleteness of the collateral compensation that will determine whether or not the signs of stagnation in the portal area will be accompanied by a general lowering of arterial pressure.

As regards the *velocity* of the blood-stream, also, the peculiar vascularisation of the liver is not without its special influence. The blood flows through the intra-lobular capillaries more slowly than in any other organ; even the medulla of bone cannot compare in this respect with the liver. One result of this is the liability of minute corpuscular substances which have entered the circulation to become arrested in this organ. Thus, on injecting cinnabar into the vessels of a frog or rabbit, the granules are found in quantity in the liver, long after they have completely disappeared from the blood. In the same way a number of pathological experiences may also be explained. Whether, indeed, the accumulation of pigment in the liver in *melanæmia* is solely determined by the retardation of the flow, is, as already stated (vol. ii, p. 696), still a matter of dispute; but the extraordinary frequency with which the liver is attacked by *metastatic processes* of the most various kinds undoubtedly depends on the slowness of the hepatic circulation. This is true both of the malignant tumour-metastases and of the infective tumours. Whatever may be the situation of a primary carcinoma, you must always be prepared to meet with metastases in the liver; while for many sarcomas, *e. g.* the *melanotic*, this organ is the classical seat of the metastatic growths. Moreover, the extreme frequency of *miliary tubercles* in the liver is known to everyone who takes the trouble to carefully examine the organ in all tubercular cases, including phthisis. This preference for the liver is also evinced by the infective processes, in the strict sense of the term. Thus, the production of *hepatic abscess* is by no means exclusively confined to those pyæmic processes which have their starting-point in the territory of the portal tributaries: in the bodies of persons who have died of small-pox, the *diphtheroid foci* (cf. vol. ii, p. 600), so termed by Weigert, are only exceptionally absent from this organ in particular. In fact, whenever a post-mortem appearance leads you to suspect that you are dealing with a bacterial affection, it should be your invariable rule to examine the liver for the presence of *colonies of bacteria.* But it is not only corpuscular materials that are, so to speak, caught up by the hepatic circulation; this gland also serves as perhaps the most ample reservoir or *storehouse for all kinds of dissolved substances.* It is an old rule in cases of poisoning to examine more particularly the liver for the poison whose presence is suspected; and as for matters which are regularly introduced into the organism or produced within it, I have already stated that the liver is one of the physiological depôts for *fat*, and shall soon have to report the same of *glycogen.* I also indicated on that occasion (vol. ii, p. 666) the special qualifications of the liver as a depository for these materials, namely, the *slowness of its blood-stream*, just referred to, and the *poverty of its blood in oxygen*, owing to the fact that, being supplied by veins, it has a markedly venous character.

We have not the same secure foundation to go upon when following the relations of the liver to the *constitution* of the blood. The inclination to attribute to this organ a share in blood-production is widely prevalent amongst writers; and it is probably owing to this that Lehmann's old analyses of the blood of the portal and hepatic veins still find a place in the text-books, although a number of more recent researches, and above all the very remarkable investigation of

Flügge,* have demonstrated the complete untenability of Lehmann's position. *Indubitable* proof even of a destruction of red corpuscles in the liver has not as yet been afforded, though the abundance of bile-pigment leaving the organ renders it highly probable. Still more hypothetical, or rather purely a matter of guess-work, is the notion already referred to (vol. i, p. 471) of a possible post-embryonic new formation of red or of colourless blood-corpuscles in the liver. All statements as to the occurrence of so-called *young* blood-cells, as well as to the relative numerical proportions of coloured and colourless elements in the blood of the hepatic vein, rest upon methods so uncertain as not to be available for scientific purposes. And since Flügge has shown that during the maximal stage of bile-formation no difference whatever can be detected even in the water-contents of the blood in the portal and hepatic veins, who could any longer expect that information would be afforded as to the hæmapoietic function of the liver by comparative examinations of the two kinds of blood, such as were carried out by Lehmann and others? So long as a practicable method is not available, we must continue groping in the dark. Pathological experience, also, which so often supplies a valuable hint, here leaves us altogether in the lurch. The diseases of the liver occupy a position to themselves. As is sufficiently intelligible from the foregoing discussion, there is scarcely another organ that so easily becomes involved in all kinds of morbid processes. But though pathological conditions of the liver are accordingly very common, it is impossible, in the great majority of cases, to say that the original disease is specially aggravated thereby. In fact, if none of the canal systems of the liver be implicated, the most extensive and profound changes may run their course in the organ without a single symptom, or with symptoms which are quite indefinite and anything but grave. Of course, that *acute necrosis* of the entire liver, such as regularly ensues on the complete occlusion of the hepatic artery and its branches,† will not be tolerated by the organism, is not surprising; but how many opportunities offer for observing the most extreme reduction of the hepatic substance, without a single indication, either during life or at the post-mortem, that might point to an essential alteration or abnormality in the constitution of the blood! Multiple tumours of all kinds, as well as echinococci, may establish themselves in such numbers in the liver, and there attain such a size, that only small portions of the proper parenchyma remain, and yet perhaps not a single symptom during the patient's life had ever indicated that by far the greater part of the liver had ceased to perform its functions. The sufferings of persons labouring under hepatic cirrhosis result rather from the interference with the portal circulation, already mentioned, than from the loss of the parenchyma of the organ, although this loss may be very extreme. Again, though individuals in whom an extensive amyloid degeneration of the liver has taken place are cachectic and anæmic, and not uncommonly dropsical, you are aware, on the one hand, that amyloid degeneration never attacks previously healthy persons; and, on the other, that besides the liver various other organs—the spleen, kidneys, intestines, &c.—are invariably involved in the degeneration. Hence, whether the cachexia should be referred even partially to the liver disease, can hardly be made out in such cases. But, however little can be made of these facts, they at least teach, in my opinion, that the organism has means at its disposal, by which the evils attending even a considerable loss of hepatic substance may, practically speaking, be perfectly compensated.

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* Flügge, 'Zeitschr. f. Biol.,' xiii, p. 133. Cf. also Heidenhain, in Hermann's 'Handb.,' v, 1, p. 241 ff.

† Cohnheim and Litten, 'Virch. A.,' lxvii, p. 153.

I do not wish, however, to make the impression that disease of the liver is, as a rule, of slight importance to the organism. We have not yet touched upon that side of the activity of the organ which is most intimately concerned in the process of digestion, namely, *the production and secretion of bile*. A theory of bile-formation is far from possible at present; we do not even know the *place* of its production with absolute certainty. The principal argument hitherto employed, namely the impossibility of detecting the specific constituents of the bile in the blood of the portal vein, has been completely robbed of its force by the investigations of Flügge; so that all that we can bring forward in evidence for regarding the liver as the place of production of the biliary substances is at bottom reducible to a solitary fact,—that these substances are not normally met with, except in the liver and in parts to which they have got access from this organ. But though ignorant of the connection of events, we are familiar with some of the details of the process of secretion. Thus, it has been determined by experiments on animals and by observation of human beings with biliary fistulæ, that bile is formed *continuously*, though in quantities which vary considerably at different times. The amount of the secretion is chiefly influenced by the *taking of food*, since in prolonged fasting it is reduced to a minimum. When the food consists of fat alone the quantity produced is very small. The amount is increased by feeding with bread and still more by a diet of flesh. The most abundant secretion, according to all observers, is produced by a mixed diet of flesh and bread. The remarkable variation in amount of the secretion according to the composition of the food, seems to me to point to the conclusion that the *quality of the portal blood* exerts an essential determining influence. It is not so much, or at least not exclusively, the augmented blood-supply through the portal vein that determines the increase of the biliary secretion. That the quantity of blood present, and the pressure, in the hepatic capillaries does exert an effect on the amount of the secretion is proved by other facts. Dogs produce less bile after a severe loss of blood, and the secretion is scanty in anæmic individuals. The considerable falling off in the production of bile which at once ensues on occlusion or narrowing of the trunk of the portal vein[*] tells in the same direction; for the interlobular veins and the capillaries then draw the whole of their blood from the much smaller hepatic arteries. If, further, the secretion is reduced both by section of the cervical cord[*] and by direct or reflex irritation of the spinal marrow,[†] this is simply the result of the fall of pressure in the hepatic capillaries which must be called forth by each of these procedures. Lastly, if the opinion held by many physicians that the biliary secretion is reduced in non-compensated cardiac lesions be correct, this would also tell for the prejudicial influence of the retardation of the blood-stream. Nevertheless, it would appear from the constant secretion of bile of normal composition, even when the pressure is lowest and the flow through the capillaries most retarded, that the dependence of bile-production on the blood-pressure and velocity is not a very intimate one.[*] Moreover, the composition of the bile is in a great measure independent of alterations in the *constitution* of the blood. True, easily diffusible substances, when they have accumulated to some extent in the blood, pass over into the bile; as, for example, urea in the uræmic;[†] sugar, when the amount contained in the blood is considerable; dissolved colouring matters, *e. g.* carmine and sulphindigotate of sodium, when injected into the blood; some of the metals, *e. g.* copper and iodine;[‡] although the statements made by many older writers with regard to quinine, ferrocyanide of potassium, and mercury, &c., have not been confirmed by recent investigators.[§] Water-drinking, according to Westphalen's observations,[||] has no influence on the amount and constitution of the biliary secretion, even when sufficient is taken to cause doubling of the urine. As for direct injection of water or salt-solution, very considerable quantities must be employed before a more abundant flow of watery bile is produced; moderate quantities, as determined by Heidenhain,[¶] do not affect the secretion at all.[**] According to some observations of Uffelmann[††] on a patient with a biliary fistula, the setting in of pyrexia appears to diminish the secretion of bile. On the other hand, we know nothing definitely as to a direct nervous influence on bile-production. Again, the many statements contained in the literature, according to which certain medicines* act as cholagogues, still require to be critically examined; and at any rate it is very necessary that the mode of action of the remedies should be accurately analysed. With regard to the secretory parenchyma, the liver-cells, it is self evident that *without them* a production of bile is impossible. Hence general necrosis of the hepatic cells, or the disintegration and disappearance of the secretory elements must necessarily put a stop to secretion, and bring about what Frerichs has termed, *acholia*. But as to how the biliary function reacts to *partial* destruction of hepatic tissue, such as occurs in the various forms of chronic atrophy, in cirrhosis, or when multiple tumours or other focal disease is present in the organ, we can at present form no opinion, because we know nothing of the degree of functional capacity of the individual hepatic cells. You will perhaps be still more interested in the question, How does the secretion behave in presence of pathological conditions in the liver-cells? The inherent difficulty of this very justifiable question is enhanced by the fact that these conditions do not in most cases involve the whole of the cells. When, for example, normal bile is secreted in advanced amyloid degeneration of the liver, it is very possibly derived from those cells alone which have remained unaffected. In *fatty liver*, which of all the diseases of this organ is most prone to attack all the cells of all the lobules, no departure from the normal has ever been detected in the constitution of the bile. As to the *amount* of the secretion in these cases, you will hardly expect us to be informed; for to this it would be necessary not merely that accident should supply us with a case of biliary fistula leading from the diseased liver, but that the appetite of the patient and all his digestive processes should be normal, that his nutrition should be good, and that he should be free from pyrexia; in short, a multitude of conditions would require to be met, such as could very rarely be found in individuals with marked fatty liver, and almost never in amyloid degeneration of the organ.

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[*] Asp, 'Ber. d. sächs. Gesellsch. d. Wissensch.,' Sitzg. July 26, 1873, p 470.

[†] Heidenhain, 'Stud. d. physiol. Inst. zu Breslau,' Hft. ii, p. 69, iv, p. 226; J. Munk, 'Pflüg. A.,' viii, p. 151.

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[*] Cf. Spiro, 'A. f. Physiolog.,' 1880, Suppl., p. 50, and especially Heidenhain's very full and accurate account in Hermann's 'Handb.,' v, 1, p. 251, *et seq.*

[†] Budd, 'Die Krankheiten der Leber,' trans. by v. Henoch, 1846, p. 296.

[‡] Mosler, 'Virch. A.,' xiii, p. 29.

[§] Mosler, ibid.; Westphalen, 'D. A. f. klin. Med., p. 588; Eichhorst, 'Neue Charité-Annalen, ii, 1877, p. 197.

[||] Westphalen, 'D. A. f. klin. Med.,' p. 588.

[¶] Heidenhain, 'Stud. d. physiol. Inst. zu. Breslau,' Hft. ii, p. 69, iv, p. 226.

[**] Cf., on the other hand, Zawilski's experiments on rabbits ('Krakauer Wochenschr.,' 1877, No. 10) referred to in Hofmann-Schwalbe's 'Jahresbericht' for 1877, Abth. iii, p. 246.

[††] Uffelmann, 'D. A. f. klin. Med.,' xiv, p. 228.

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* Budd, l. c., p. 35. Cf. also Hoppe-Seyler, 'Physiolog. Chemie,' p. 286. The most trustworthy and comprehensive statement is that of W. Rutherford, 'Brit. Med. Journ.,' 1878, p. 945, and especially 'Transact. of the Roy. Soc., Edinburgh,' xxix, p. 133.

What I have been able to tell you of the pathology of the biliary secretion does not, you see, amount to much. If we leave out of account the mixture of various soluble substances with the bile, already referred to, we know hardly anything of its chemical constitution in morbid conditions, that might not almost be included with mere physiological variations in concentration, relative contents of the bile-acids, and of the various pigments, &c.* As regards its amount, however, I desire to state emphatically that we are acquainted with no facts which would justify the idea familiar to the old physicians of a pathological "*polycholia*." The quantity of bile produced in twenty-four hours varies much, according to the individual's diet, the size of his body, and above all the size of his liver; so much so that, as you are aware, the amount of the secretion is always calculated by the physiologist for a liver weighing one kilogram. Accordingly, there is no doubt, of course, that persons with very large, or, as they may be called, *hypertrophic* livers produce a more than average amount of bile. But such livers are found only in big, strong, well-nourished people, who are in the habit of eating large quantities of food, and whether the bile secreted by these individuals is really in excess of the amount required and employed in digestion is very far from proved; only when excessive, however, would it be correct to speak of a pathological polycholia. While, then, there is no scientific basis for the symptoms ascribed to the alleged polycholia, the evidence for the occurrence of severe symptoms in its opposite extreme, *acholia*, is very little better. I am not inclined to deny, you are aware, that there may be a falling off or a cessation of bile-production under pathological conditions, nor do I dispute that digestion will be impaired by certain evils, shortly to be discussed, which are occasioned by the absence of bile from the intestine. But acholia is chiefly interesting, not from the digestive disturbances occasioned by it, but from the possibility that suppression of the biliary secretion may be *per se* of essential importance for the organism. Older writers regarded this as self-evident, and consequently spoke of a special form of *jaundice due to suppression*. Frerichs* has recently reconstructed his view of the clinical picture of acholia; it is not the retention of the fully formed biliary constituents in the blood, but of materials destined to contribute to this secretion, that is regarded by him as one of the factors to which are attributable the signs of profound blood-intoxication, and especially the severe disturbances of the nervous system, occurring in acute hepatic atrophy and other processes leading to destruction of the parenchyma of the liver. A precise reply to the questions raised by this theory is not in my opinion at present feasible, having regard to our ignorance of the connection of events in the secretion of bile. Still icterus by suppression has not been able to hold its ground since the clinical material was subjected to a more accurate anatomical and physiological analysis; and as for acute atrophy of the liver, Frerichs† himself lays stress on the fact that, by the destruction of the hepatic cells, not only is the biliary secretion but "every other action, which this powerful organ exerts on the metabolic processes, suspended, while the products of the disintegration of the glandular substance pass over into the blood." Hence, if in the diseases now under discussion, the liver really forms the starting-point and centre of the entire process, no satisfactory conclusion, it is evident, can be drawn therefrom as to the consequences of an abeyance of the biliary secretion, or acholia. But if you bear in mind what I formerly told you of the comparative unimportance of very extensive chronic atrophies and degenerations of the liver, you may consider the view that acute hepatic atrophy is not a primary disease of the liver as at any rate open to discussion.

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* Sokoloff, 'Pflüg. A.,' xii, p. 54.

As compared with our knowledge of bile-formation, we are well acquainted with the mechanism of *its discharge*. When dealing with the saliva and gastric juice, there was no need to distinguish between the two acts of secretion and discharge; but this is decidedly necessary in considering the bile. Saliva and gastric juice are not constantly produced, but only under the influence of particular stimuli, and the fluids are at once poured out into the mouth and stomach respectively. The secretion of bile, though it varies greatly, is *continuous*, and is no less continuously forced onwards through the bile-ducts by the pressure of the fluid behind it, *i. e.* under the pressure of secretion, aided slightly by the movements of respiration. But its discharge into the intestinal canal is very far from continuous, and takes place *at certain periods and in quantities at a time.* This is rendered possible, as you know, by the presence of a *reservoir*, which in all animals is provided, in some measure at least, by the roomy *large bile-ducts*, and in man and many species by an additional organ, the *gall-bladder*, specially adapted to this purpose. In this bladder, the bile gradually accumulates during fasting, and usually fills it to distension at the commencement of the next meal. The discharge of the bile from the reservoirs containing it occurs at once, when intestinal digestion begins, by means of the contractions of their muscular walls. The contractions are initiated partly by simple extension of the peristaltic movements of the duodenum to the bile-ducts, but mainly by a reflex which is excited by the contact of the acid chyme with the papilla of the ductus choledochus. Thus, a large quantity of bile is at once poured out over the chyme, and so long as the contents of the stomach continue to enter the duodenum, they become mingled with the bile, which is now secreted in profusion and continually discharged. The evacuation of bile only ceases when the duodenum is perfectly empty, but from this time till the next meal, not a drop enters the intestine; the bile is received by the reservoirs, and chiefly by the gall-bladder.

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* Frerichs, 'Klinik d. Leberkrankheiten,' 2 Aufl., i, p. 202.

† Frerichs, l.c., p. 240.

While the secretion of the bile and its movement forwards along the biliary capillaries is continuous, its accumulation in the reservoirs will depend simply on their accessibility. Since one set of reservoirs, the large bile-ducts, form the passages for the discharge of the bile into the intestine, their imperviousness involves at the same time an impediment to evacuation, and will be best discussed in connection with such impediments. It is not so with the gall-bladder which is situated laterally. Its cavity may be very considerably encroached upon by large gall-stones or by projecting tumours, or its lumen may be contracted by cicatrices—the residues, as a rule, of chronic ulcerative processes set up by the gall-stones,

—so that very little bile can be accommodated in it. It becomes completely *impervious* to bile, if the cystic duct is compressed or obstructed by tumours, cicatrices, or—as is by far the most common cause—by *impacted gall-stones.* In cases of this kind no bile can enter the bladder from the moment of occlusion, nor can any escape from it, though the organ may be filled to distension, especially in cases of impacted gall-stone. The contents of the occluded gall-bladder do not, however, long continue bilious. Diffusion takes place between them and the contents of the blood-vessels and lymphatics of the wall, more especially the latter, and while water and albumen enter the sac, *the specific constituents of the bile are diffused outwards.* The bile-pigment escapes first, so that after a few weeks the fluid of the occluded bladder is colourless, without a trace of pigment, but contains a considerable quantity of salts of the bile-acids, fat and cholesterin.* Twice or three times as long a period must elapse before the bile-acids have disappeared. In the meantime the fluid contents are considerably increased, owing partly no doubt to continued secretion by the mucous glands; and as the result there is finally developed the condition familiar to the pathological anatomist under the name of *hydrops cystidis felleæ.* The gall-bladder is now much enlarged, forming a pyriform, distended sac, which may not infrequently be felt during life through the abdominal wall. As is usual in cysts with an epithelial lining, its contents consist of a colourless, slightly tenacious, watery solution of albumen, mucus and salts, with some fat and cholesterin. As regards digestion, it makes little difference whether the imperviousness of the gall-bladder is due to an encroachment on its cavity, or to occlusion of the cystic duct; in both cases an accumulation of bile in the bladder during the intervals between digestion will be impossible. The human being is thus placed, in this respect, on a par with the horse and elephant, and such other mammals as are *unprovided with a gall-bladder.* Owing to the much longer period occupied in digestion by these animals, most of which are herbivora, a periodical accumulation is certainly much less important than in man with his regular and prolonged intervals between digestion. Moreover, in many animals, *e. g.* the elephant, the peculiar sacciform dilatation of the ductus choledochus before entering the intestine supplies the place of a gall-bladder. In man too, as might be inferred *a priori*, the ductus choledochus and hepatic ducts may partially assume the *rôle* of the gall-bladder; for these ducts usually display a moderate dilatation in imperviousness of the ductus cysticus. That they could ever contain the 40—50 c.cm. bile which may be accommodated by the gall-bladder, is not of course to be expected; and people with impervious gall-bladders no doubt lose part of the advantage which accrues to intestinal digestion from the admixture of an abundance of bile with the chyme the moment it enters the intestine.

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* Ritter, 'Journ. de l' anatomie et de la physiologie,' 1872, p. 181.

The arrangement in virtue of which the bile is not, in a normal condition, at once discharged, but collected in the receptacles set apart for it, has an additional interest in pathology, because it is extremely favorable to the development of *biliary stagnation.* A slight degree of stagnation must even result, when a rather long interval passes between two meals. Its occurrence in the gall-bladder will be furthered by flexion and dislocation downwards of this sac, such as commonly results from tight lacing; the *efflux from the bladder,* though not the entrance of bile, will then be *impeded.* Feebleness of the muscular coat of the gall-bladder, which is probably not an uncommon condition of advanced life, must obviously facilitate the production of stagnation. And you will shortly learn that the same result may attend a large number of pathological agents, in a stricter sense, by which at the same time the entrance of bile into the intestine is impeded. In every instance, biliary stagnation, however conditioned, leads first to inspissation of the bile, whereby it becomes dark and viscid, or may almost lose its liquid consistence. Bile of this kind is obtained, *e. g.* from a *complete* fistula of the gall-bladder—one, *i. e.* in which the d. choledochus is at the same time occluded—when the escape of bile has been prevented for a time. If the stagnation persists long, the concentration may become so considerable that cholesterin and bilirubin separate out; and for this reason it was formerly supposed that the *concretions* so commonly present in the gall-bladder and more rarely in the bile-ducts were also caused solely by concentration of the bile. This, however, is an error, since gall-stones always contain ingredients which do not occur in normal bile. As is well known, gall-stones are grouped in *two classes*, according as they are *rich or poor in cholesterin*. Those of the latter class are small, irregular, dark brown or dark green, almost black masses with a faint lustre, while the much commoner stones of the first category either consist almost altogether of cholesterin and have a distinctly crystalline fracture and alabaster-like appearance, or display alternating layers, pigmented and white. All large stones and all having an approximately globular or regularly angular form, with smooth, often facetted, surfaces, are rich in cholesterin. For the finer details of structure, and especially the chemical composition of gall-stones, I must refer you to the pathologico-anatomical and chemical literature of the subject,* while I confine myself to the points in which the constituents of gall-stones differ from those of normal bile. The bile-pigments occurring in all gall-stones—for the apparently pure cholesterin form has practically always a pigmented nucleus—do not exist *free* or as easily soluble alkaline combinations; they are always united with *lime* and *magnesia*: even the finest gravel found in the smaller ducts always consists of bile-pigment combined with lime. In the second place, however, besides the normal colouring matters —bilirubin and biliverdin—others are commonly present. These have been minutely investigated by Städeler, and termed *bilifuscin*, *bilifulvin*, and *bilihumin*; they must certainly have originated in chemical transformations of the normal pigments. Moreover, the occurrence of antecedent decompositions is borne out by the presence of substances giving the reactions of the bile-acids but insoluble in water, and consisting mainly of so-called *choloidinic acid*. You must admit that the appearance of all these substances cannot be explained by a simple concentration and inspissation of the bile;

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* H. Meckel von Helmsbach, 'Microgeologie,' 1856, p. 44, *et seq*. Frerichs, loc. cit., ii, p. 466; Klebs, 'Handb. d. pathol. Anat.,' i, p. 486; Städeler, 'Vierteljahrschr. d. naturforsch. Gesellsch. in Zürich,' 1863, viii, p. 1; Kühne, 'Physiol. Chemie,' p. 83; Maly, 'Wien. Akad. Sitzungsber.,' Bd. 70, Abth. iii, Juli, 1874; 'Annal. d. Chemie und Pharmacie,' Bd. 175, p, 76; Hoppe-Seyler, 'Physiol. Chemie,' p. 319.

they evidently show that a *decomposition* of the bile must have preceded their formation. The accumulation of cholesterin in quantities is also most simply understood on the assumption of a splitting up of its solvent, the bile-salts. As to the cause of this decomposition, however, we are far from adequately informed in individual cases. It was very natural to take refuge in inflammation, that convenient helper of pathology, and to suppose that a catarrh of the gall-bladder or ducts exerts, by the mucus secreted in it, a fermentative action on the bile-salts and so splits them up. But there is not a particle of proof of such an occurrence, and when the wall of a gall-bladder containing calculi is found inflamed, the contrary explanation—a cholecystitis called forth by the presence of the stones—is certainly the correct one. Again, the mucus supposed to form the primary nucleus of the calculi cannot be demonstrated.* The occasional existence of a nucleus formed by a foreign body which has entered the gall-bladder throws no light on the infinitely commoner cases where no such body is present; for the tendency observable in many individuals to the formation of new stones, persisting for years and tens of years, indicates that the agents initiating the decomposition of the bile must recur frequently. Thénard suggests that in the subjects of biliary calculi the sodium-contents of the bile are abnormally reduced. Klebs believes that the production of an acid secretion by the mucous membrane of gall-bladder may be the determining factor. In fact, it will be judicious to constantly bear in mind that bile, and especially the bile-salts, are very readily decomposable, so that decomposition may be initiated by very different factors. But when it has once set in, choloidinic acid and the combinations of lime with bilirubin-derivatives are precipitated, and upon them the cholesterin is deposited in layers. While, accordingly, the *process of "stone-formation"* is very far from identical with simple biliary stagnation, it is yet obvious that stagnation will be extremely favorable to the formation of stones. It will certainly be still more serviceable to the *growth* of calculi; and there is no doubt, I think, that biliary concretions could scarcely exceed the bile-gravel in size without the aid of stagnation. If, in connection with this fact, you consider what I have just told you as to the commoner causes of stagnation in the gall-bladder, you will hardly attribute it to accident, that biliary calculi should occur by preference, on the one hand, in women, and, on the other, in advanced life.

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* Kühne, l. c., p. 86.

In order, however, that the bile accumulated in the reservoir, as well as that freshly secreted during digestion, may actually reach the intestine two conditions have still to be fulfilled. In the first place, *the continuity of the wall of the canal,* through which the bile has to pass, *must nowhere be interrupted;* in the second place, the passage must be *pervious and unobstructed.* A trauma may sometimes be the cause of a solution of continuity of the wall of the bile-passages, and both punctured and incised wounds, as well as laceration, have been observed in the gall-bladder and large ducts. Much more commonly, however, the rupture or *perforation* is brought about by chronic ulcerative processes, mostly due to the presence of stones. The formation of such abnormal openings must under all circumstances result in *the escape of bile;* but the importance of this event differs extremely, according to the locality into which the aperture leads. Communication with the surface through the abdominal wall so as to produce a regular external *biliary fistula,* such as since Schwann's initiative, is artificially established by the physiologist, is quite exceptional. Direct perforation into the peritoneal cavity is fortunately also rare. Fortunately, I say, because in the vast majority of instances a fatal peritonitis follows the perforation by an ulcer of the gall-bladder or the ductus choledochus. Peritonitis need not necessarily result, it is true: it is an everyday experience with the experimental physiologist that the escape of a little bile into the peritoneal cavity during the establishment of a fistula is followed by no disadvantage to the animal experimented on; and it is not long since I had an opportunity of observing a case of traumatic rupture of the left hepatic duct, which likewise ran a comparatively favorable course. In this case, bile escaped from the left posterior angle of the quadrate lobe, at which spot the rupture was situated; directly on the occurrence of the trauma and for weeks afterwards it trickled into the cavity of the abdomen, from which on several occasions very considerable quantities were removed by tapping. At the same time the heart's action was slow, and skin and urine icteric. After several months, however, the signs of bile-absorption disappeared, although physical examination of the abdomen showed beyond doubt that a considerable quantity of fluid was present in the cavity. This fluid was proved by the chemical examination of portions obtained by puncture and afterwards at the autopsy—death having taken place as the result of an intercurrent affection—to actually consist of a mixture of lymph and bile. The autopsy also showed that the entire surface of the visceral and parietal layers of the peritoneum was covered by a firmly adherent, perfectly regular layer of new-formed connective tissue, brown in colour from the presence of granular and amorphous bile-pigment, and consisting, on microscopic examination, of tightly packed bundles of beautiful spindle-cells. The non-occurrence of bile-absorption from the abdomen during the last few weeks of life was clearly attributable to the existence of this membrane.* But although in this instructive case the bile which escaped in such profusion into the peritoneum produced an adhesive instead of a purulent inflammation, an equally favorable course can scarcely ever be expected in ulcerative perforation. For the escape of bile is here always preceded by a necrosive and suppurative process, and if, as is usual, the ulceration depends on the irritation of gall-stones, you know that the bile entering the abdomen will have previously undergone decompositions and will probably not be so harmless as the perfectly normal secretion. Nature adopts another method in these cases, and seeks to avert the general and fatal peritonitis by setting up a circumscribed inflammation which leads to the production of adhesions between the portion of gall-bladder involved and some other organ. If perforation subsequently occurs the abnormal communication is established with this organ and not with the cavity of the peritoneum. Complete external biliary fistulæ may be produced in this way; but much more commonly the perforation leads into the duodenum, whether the ulcerative process has started in the gall-bladder or in the bile-ducts. Abnormal communications originating in this way have been observed, often with the colon, in a few cases with the stomach, with the pelvis of the right kidney, with the right pleural cavity or right bronchi after previous adhesion to the diaphragm, and even rupture into the portal vein has been described by trustworthy writers.[*] Of all these, communication with the duodenum is unquestionably the most favorable, since this is the region which normally receives the bile. Even when the abnormal passage permits the entrance of gall-stones as well as bile into the duodenum, this is as a rule a desirable event, since the organism can thus most conveniently rid itself of the stones. But its consequences may be evil when the stone is very large, for the latter may then become impacted in a coil of intestine and give rise to fatal obstruction of the bowel;[†] small stones, on the contrary, can only prove dangerous by entering the vermiform process. But except for these unfortunate accidents, it is evident that the duodenal is less disadvantageous than any of the other fistulæ, since all biliary fistulæ, with this one exception, *involve a loss of bile for intestinal digestion.* The quantity lost may differ greatly. Such a large escape has sometimes been observed from external fistulæ, the stools being at the same time clayey and quite uncoloured, that it was considered justifiable to assume that all the bile had selected the abnormal path, and to utilise these cases for quantitative estimations of the bile secreted in twenty-four hours.[‡] Schiff claims to have repeatedly convinced himself that when a wide artificial fistula is established, the whole of the bile escapes externally, none entering the intestine.[§] But not unless the aperture is wide and gaping, and in ordinary fistulous communications the characteristic colour of the fæces proves that the intestine contains bile. Hence interruptions of continuity of the bile-passages, though often accompanied by striking symptoms, have not usually the same significance for digestion as have *the obstacles which impede the passage through the ducts*, or render them completely impervious.

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* According to a communication by Thiersch at the "Chirurgencongress" of 1880. Cf. also Uhde, 'A. f. klin. Chirurg.,' xxv, p 485.

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[*] Frerichs, l.c., ii, p. 507.

[†] Frerichs, l. c., ii, p. 504; Cohnheim, 'Virch. A.,' xxxvii, p. 415.

[‡] Westphalen, l. c.; J. Ranke, 'Die Blutvertheilung u. der Thätigkeitswechsel d. Organe" 1871; Wittich, 'Pflüg. A.' vi, p. 181.

[§] Schiff, 'Pflüg. A.,' iii, p. 598.

Such obstacles exist in great variety. *Stones* may become impacted in any of the larger bile-ducts, most frequently in the ductus choledochus. *Animal parasites* may block their lumen; *e. g.* distomata or echinococci which have penetrated them from the liver, and occasionally ascarides from the intestine. *Tumours* often render a bile-duct impassable. Thus, a carcinoma of the duodenum, of the ductus choledochus itself, of the head of the pancreas, or of the epigastric lymphatic glands may obstruct the ductus communis; enlarged lymphatic glands in the portal fissure may compress the hepatic duct; while single branches of this duct may be occluded by tumours situated in the liver itself. *Cicatricial strictures* of individual ducts, most frequently the choledochus, may arise from antecedent ulcerative processes, and in cirrhosis of the liver, the intra-hepatic bile-ducts are constricted by contracting bands of connective tissue. Lastly, total obliteration or absence of the large external bile-passages has been several times observed as a congenital malformation. These are all such factors, you perceive, as may be exactly paralleled in every canal-system of the body. Still the low pressure under which the bile is secreted and discharged, makes it possible for the flow to be arrested by resistances which could not act as obstacles elsewhere. By far the most common impediment to the efflux of bile is ordinary simple *gastro-duodenal catarrh,* which at the same time implicates the portion of the ductus choledochus included in the wall of the intestine,—Virchow's portio intestinalis. The swelling of the mucous membrane of this portion, together with the product of the catarrh, the well known *mucous plug,* is quite sufficient to prevent the entrance of bile into the intestine for days together. But under certain circumstances the mucous plug and catarrhal swelling are not necessary. In a starving dog, the persistent firm contraction of the duodenum is apparently capable of completely arresting the flow: after several days' starvation, the animal invariably becomes slightly jaundiced—an occurrence which, it is true, Kunkel* ascribes to occlusion of some of the larger bile-ducts by peculiar flakes, separated out from the bile produced during starvation. In man, too, it appears very probable that a definite, very commonly occurring kind of icterus depends upon an interference with the escape of bile by the non-inflamed ductus choledochus: I refer to the *jaundice* which attacks such a considerable percentage *of new-born children* during the first few days after birth. If this affection really depended, as has been claimed, on the altered relations of the circulation of the liver, or was of hæmatogenous origin and produced by the extreme alteration of the vital conditions, it must necessarily be met with in all new-born children. It is far from universal, however, occurring only in about 60 per cent. of births, and this fact, in my opinion, gives more plausibility to the view that it is due to mechanical causes. During intra-uterine life, as proved by the meconium, true bile is secreted and discharged into the intestine; but the slight degree or absence of icterus in children who come into the world with an obliterated ductus choledochus proves that the production of bile during this period is extremely scanty. This condition of affairs is suddenly changed after birth, so soon as the child takes its first nourishment and begins to breathe. The idea most obviously suggesting itself in these cases is, I think, that the capacity of the narrow ductus choledochus does not in all individuals admit of an immediate accommodation to the considerably increased flow of bile: a portion only escapes, the remainder being retained for a time. By this explanation, one of the objections commonly raised to the mechanical character of the jaundice, *i.e.* the absence of the mucous plug in such of the children as die icteric, is completely deprived of cogency; while the second objection, based upon the absence of bile-pigment from the urine in most cases, is disposed of by the fact brought to light by Orth*, that the kidneys of all the children dying during the attack of jaundice, contain *a crystalline deposit of bilirubin*. Nay more; since Birch-Hirschfeld† discovered that both bile-pigment and *bile-acids* may be detected in the pericardial fluid of icteric children by Neukomm's process, there is no longer any reason to doubt the mechanical nature of the jaundice.

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* Künkel, 'Pflüg. A.,' xiv, p. 367.

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* Orth, 'Virch. A.,' lxiii, p. 447.

† Birch-Hirschfeld, 'Virch. A.,' lxxxvii, p. 1.

It is true that Violet* has recently sought to support the notion of its hæmatogenous origin by the fact that children in whom the umbilical cord is tied late, and who are in consequence polyæmic (cf. vol. i, p. 426), more often develop a marked degree of icterus than do those in whom ligation is early carried out; but this may perhaps be explained on the supposition that bile-production in these very children is unusually abundant. The cause of the jaundice by absorption, is believed by Birch-Hirschfeld to be *compression of the bile-ducts owing to œdema of the peri-portal cellular tissue*; and the œdema he takes to be the consequence of stagnation due to the cessation of the circulation through the umbilical vein, and to a possible delay in the regular development of the pulmonary circulation. Without desiring to discuss the justice of this interpretation, it appears to me that we must wait for a larger experience as to the frequency of œdema of Glisson's capsule. I have recently examined the bodies of new-born children with ordinary icterus, in which there was no œdema of the capsule, so that I am unable to agree with Birch-Hirschfeld in attributing such exclusive importance to this condition. Whether, in addition to the intestinal portion of the ductus choledochus, other portions of the ducts can be made impermeable as the result of simple catarrh, appears more than doubtful. The larger ducts, whose liability to catarrhal inflammation cannot be disputed, are too wide to admit of occlusion by catarrh, and catarrh has never yet been demonstrated in the smaller ducts. But bearing in mind the very slight tension under which the bile moves forwards through these finer ducts, it is certainly worth considering whether they might not be compressed by vessels filled to distension with stagnant blood; and whether the icterus, which though slight so often acccompanies insufficiently compensated cardiac lesions may not depend on such compression of the interlobular bile-ducts.

As to the significance of these impediments, it makes not a little difference whether the passage is partially obstructed or fully impervious, and the *seat of the occlusion* is also of considerable importance. Closure of the ductus choledochus or of the hepatic trunk completely arrests the flow into the intestine. Occlusion of branches of the ductus hepaticus simply blocks the way for the bile collecting in and travelling along these channels, but does not disturb the efflux from the remaining branches. Accordingly, such intra-hepatic impediments are almost equivalent, so far as intestinal digestion is concerned, to narrowing, not closure, of the common bile-duct.

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* Violet, ibid., lxxx, p. 353.

The effects on digestion of a reduction or cessation of the supply of bile to the intestine will appear most clearly on considering what the bile normally accomplishes in the intestine. Of primary importance is its influence on the *digestion of fats*. The power it possesses of dissolving small quantities of fat is not of practical significance ; its chief function is the conversion of the fats into *a very fine emulsion*, in which it is assisted by the movements of the intestine. The emulsion is particularly fine and lasting when the emulsifying action of soaps participates in its production ; and the presence of soaps in the intestine is also provided for by the bile, which easily and rapidly saponifies the fatty acids, separated from the neutral fats by the pancreatic juice. To these two functions must be added a third—that the bile essentially facilitates the passage of the emulsified fat through the moist intestinal wall into the radicles of the chyle-vessels ; for, like a soap-solution, its adhesion for oil is greater than for water : oil, which passes through a membrane moistened with water only under high pressure, will filter through one moistened with bile in the absence of all pressure.[*] It is not to be denied that we are no longer justified in attributing to these facts that importance in the digestion of fats which they recently appeared to claim. For Will[†] and Cash,[‡] working independently, found, in the frog and the dog respectively, that no emulsion is present in the intestine during the digestion of fats. Indeed, the latter observer regularly found that the entire contents of the intestine were acid, so that an emulsion could not possibly exist there, and yet the chyle-vessels of the dog were at the same time filled with typical white chyle. Proof was therefore afforded that fat-absorption from the intestine may take place without previous emulsification of the neutral fats. But although the manner and method of the action of the bile in fat-digestion appears to require further investigation, the fact of such action cannot be doubted in presence of the physiological and pathological experiences shortly to be discussed. As compared with this function, its influence on starches and sugar, and upon carbohydrates generally, may be neglected. Albuminous substances are not directly affected by it; nevertheless its utility in the digestion of albumen must not be depreciated, for it precipitates the peptones and the dilute acid solutions of albumen, *i. e.* all the solutions of albumen, which enter the intestine from the stomach: at the same time it *throws down the pepsin*, and consequently puts a stop to peptic digestion. As regards other effects of the bile in the digestive canal, we know that it *stimulates the peristaltic movements:* very small doses of bile-salts, if introduced into the stomach or the blood of a dog, will give rise to vomiting and diarrhœa.* Lastly, it is capable, not indeed of preventing, but of *delaying the putrefaction* of substances present in the intestines.

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[*] Steiner, 'A. f. Anat. u. Physiol,' 1873, p. 137, 1874, p. 286.

[†] Will, 'Pflüg. A.,' xx, p. 255.

[‡] Cash, 'A. f. Physiolog.,' 1880. p. 323.

Accordingly, it will be *the digestion and absorption of fats* that will chiefly suffer as the result of a deficiency of bile. And, indeed, the result of hundreds of observations, both at the sick bed and on animals, is that the less the quantity of bile entering the intestines the smaller is the amount of fat absorbed. A dog whose ductus choledochus has been ligatured, or a man in whom the duct is occluded from some cause or other, and living on a mixed diet containing fat, passes fæces containing such an abundance of fatty matter that the stools resemble clay in colour, being grey, or even white and glistening. Nor is the defective fat-absorption capable of correction by the pancreas and its secretion. In many cases of icterus, and especially in the commonest form of all, that depending on gastro-duodenal catarrh, the pancreatic duct, which enters the intestine with the ductus choledochus, is also occluded. Even in those instances where the bile is arrested by some impediment in the choledochus before its entrance into the intestine, and the pancreatic juice is freely discharged, the action of the latter fluid will be impaired by a factor the knowledge of which we owe to Kühne.* This is nothing else than the capacity of the gastric juice to completely digest the pancreatic ferment; and it is consequently clear that only the precipitation of the pepsin by the bile can protect the pancreatic ferment from destruction, and make its action in the intestine possible. The slight degree of opalescence of the chyle-vessels in dogs with ligatured ductus choledochus, in spite of an abundant supply of fatty food, also shows very strikingly that, in the absence of bile from the intestine, the pancreatic juice cannot be of much service to fat-absorption. Moreover, owing to the great value of the trypsin as the agent in the digestion of albuminous substances in the intestine, a very serious additional disadvantage must arise from the relationship just touched upon: in the absence of bile less albumen also will be worked up and absorbed. Further, there is constantly a tendency to *constipation* in persons through whose intestines little or no bile flows; the clayey stools have a most offensive odour, and in the intestines there is a considerable *development of gas*, so that such patients usually complain of flatulence—all of them symptoms which might be directly inferred from the functions of the bile already described. This is all we know of the effects of a deficiency of bile on digestion; our knowledge does not allow of our saying more. So long, in particular, as we are not better informed both as to the fate of the bile in the intestine, and the further changes undergone by the albumen precipitated by the bile, all further consideration of other possible consequences to digestion, arising out of a deficiency of this fluid, would be nothing but idle speculation.

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* Schülein, 'Zeitschr. f. Biol.,' xiii, p. 172.

But the effects of such deficiency which have been already dwelt on, and are certainly established, evidently suffice to constitute a most serious condition for the entire organism. An individual who cannot absorb enough fat to replace that which is constantly being consumed, must of necessity emaciate unless he can procure the required fat by the splitting up of albumen. To do this, however, even with a perfectly normal digestive apparatus, very large quantities of albumen must be taken as food; how much more would be needed when the function of the pancreas in digesting albumen is so greatly interfered with! As a matter of fact, it is impossible for a dog with a complete biliary fistula to keep up its weight and normal nutrition except by consuming enormous quantities of flesh. The animals regularly become enormous eaters, the more so because the loathing which quickly appears on a purely flesh diet makes it necessary to add large quantities of carbohydrates to the food.

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* Kühne, 'Verhandl. der Heidelb. naturforsch. Gesellsch.,' 1876, N. F. 1, p. 190; Mays, 'Untersuchungen d. Heidelb. physiol. Inst.,' iii, p. 379.

A few cases of biliary fistulæ have been observed in man also, where the nutrition, for a time at least, was good and unreduced, although the condition of the fæces proved that no bile entered the intestine. In the vast majority of such cases, however, compensation such as is possible in dogs, is absolutely out of the question. True, in the human subject, the absence of bile from the intestine is much less frequently due to a fistulous opening than to imperviousness of the bile-passages; and on considering, for example, the most common cause of this imperviousness, namely, gastro-duodenal catarrh, you will find that the ensuing loss of appetite and functional disturbance of the stomach render a compensation by increased digestion of albumen impossible. But even if we leave this complication out of account, the experience of all experimenters that dogs do not bear simple ligature of the ductus choledochus so well as the combination of this operation with the production of a fistula of the gall-bladder indicates that the disadvantages arising from the absence of bile in the intestine are considerably intensified by the retention of the secretion in the organism.

In order to estimate exactly the evils which attend *the retention of the secreted bile*, it will first of all be advisable to determine whether, after the efflux is prevented, bile continues to be secreted, and if so whether in amount and composition it remains as before. Of course no conclusion can be arrived at from the extreme fulness of all the receptacles, gall-bladder and bile-ducts, which is found a short time after the closure of the ductus choledochus; for not till the tension of the bile collected in the ducts has acquired a certain elevation can the occlusion exert an influence on secretion. More importance is therefore to be attached to the discovery of *ectasis of the bile-passages* after *long* occlusion of the ductus choledochus, an ectasis which may even extend to the interlobular ducts, and is not uncommonly so marked that branches of very small size acquire the diameter of a normal ductus hepaticus or more. The contents of the dilated ducts are usually very concentrated, and sometimes partly consist of gravel, but in other respects resemble normally constituted bile. Such an ectasis is found only when the efflux of bile has been long and absolutely prevented; and should you ever have an opportunity of examining the body of a person who during several weeks preceding death has suffered from catarrhal icterus you will seek for dilatation in vain. In simple catarrhal icterus, however, the exclusion of the bile from the intestine can hardly ever be absolute, and more especially continuous, from beginning to end; to this must be added the fact, that from want of appetite for food and imperfect nutrition very little bile is produced by such patients. The circumstance that the impairment of nutrition caused by absence of bile from the intestine is necessarily followed by a reduction of the biliary secretion, possesses a high degree of importance for the question now occupying our attention. It may indeed be regarded, as will shortly appear, to be a kind of self-help of the organism. We shall not enter upon the vexed question of the influence on the biliary secretion of the absorption of bile from the intestine;* but we may venture to assert that after the escape of bile has been arrested, it still continues to be produced in perfectly normal fashion, except that in most cases its quantity is reduced. The extent of the reduction is, it is true, unknown to us; for the quantity of bile accumulating in the ducts when the occlusion is absolute affords no indication of the amount secreted, since, owing to the increased tension in the ducts, not merely is the water of the bile absorbed, but all its other constituents as well.

The absorption takes place exclusively by means of the *lymphatics*. After ligature of the ductus choledochus, Fleischl† succeeded in detecting bile-acids in the lymph, before they could be discovered in the blood; while Kufferath* found that they were altogether absent from the blood when the ductus thoracicus was also occluded. It is very probable that the absorption commences from the large bile-ducts. This would appear to be so from the observation of Heidenhain,† that a solution of indigo-carmine introduced from a biliary fistula into the bile-ducts under a certain amount of pressure stains the mucous membranes, fasciæ, skin, &c., much more rapidly than it stains the liver itself. But when the occlusion of the bile-passages persists for a time, the finer canals also allow of absorption. Of this I was able to convince myself recently in the case of a dog with artificial stenosis of the ductus choledochus: although the conjunctivæ and the urine were intensely icteric till the time when the animal was killed, the sole contents of the dilated *large* bile-ducts were a perfectly *colourless* fluid, rich, however, in cholates and cholesterin. The bile after absorption passes through the ductus thoracicus and is distributed through all parts of the body. The distribution of the *bile-pigment* may be most readily followed. Before twenty-four hours have passed the blood-serum has acquired a distinctly yellow hue; the transudation of all parts rapidly becomes altered, giving rise to a diffuse saturation of the tissues with biliary colouring matter. But for the colour to become strikingly noticeable, a certain degree of concentration is necessary; hence it is that the staining of the conjunctivæ does not usually appear before the third day, and that of the skin still later. The longer the obstruction of the bile-passages and the absorption last, the more intense does the *icteric coloration* of the tissues become. The skin by degrees acquires a deep yellow hue, which may even have a tinge of olive in it, and in very extreme cases a bronze or greenish shade, completely justifying the name of *icterus viridis* or *melas*. All the internal membranes and most parenchymatous organs and tissues become stained, though not in an equal degree. Those which are ill supplied with blood- and especially lymph-vessels, like cartilage, the cornea, and the peripheral nerves, remain unaffected; the substance of the brain and spinal cord also

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* Huppert, 'Arch. d. Heilk.,' 1864, p. 237; Schiff, l. c.; Sokoloff, 'Pflüg. A.,' xi, p. 166; Kunkel, l. c.; Tappeiner, 'Wien. akad. Sitzungsber.,' lxxvii, Abth. 3, 1878, April-Heft; 'Mittheilung. aus d. Münch. pathol. Inst.,' 1878, p. 218.

† Fleischl, 'Arb. d. Leipz. phys. Anst.,' 1874, ix, p. 24.

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[*] Kufferath, 'A. f. Physiol.,' 1880, p. 92.

[†] Heidenhain, 'Stud. d. physiol. Inst. zu Breslau,' 1864, Heft iv, p. 233.

retains its natural colour. Any chance inflammatory exudation will of course be stained, and the same may be said of a number of secretions. The bile-pigment does not, however, pass over into all the secretions: the saliva, the tears, the gastric and pancreatic juices, and also mucus, do not become icteric. The bile-pigment is dissolved in the fluids, just as it is in the blood; and the tissues also owe their icteric coloration in the first instance to diffuse *imbibition* with the colouring matter. In the skin the rete Malpighi is chiefly affected and then the cutis, and it is probable that the unequal capacity for imbibition of the various tissues has a certain share in producing the unequal intensity of the staining. But in cases where the icterus is prolonged or especially severe, solid pigment is also met with. It will at first have the form of fine, and later on of coarse particles, which are angular or irregularly rounded in shape, yellow, brownish, or greenish yellow in colour, and undoubtedly represent insoluble combinations of bile-pigment or its derivatives. These pigment-molecules are met with earliest in the liver, especially in the central zones of the lobules, and here they are also wont to be most numerously deposited. After the liver, they are most usually met with in that organ which is chiefly concerned in the removal of the bile-pigment from the body, namely the *kidney*. As might be anticipated in the case of so diffusible a substance, excretion from the kidneys begins very early, and although the dark hue acquired by the urine very shortly after occlusion of the ductus choledochus depends partly on an increase of the ordinary urinary pigment,* it usually gives, even after forty-eight hours, the unmistakable reaction of bile-pigment. The quantity of bile-pigment thus excreted is usually directly proportional to the intensity of the icterus: in mild cases the urine is saffron-yellow to red-brown, but in severer ones dark-brown, or even black-brown in colour. In icterus neonatorum, also, bile-pigment is excreted by the kidneys. In severe cases where the children perish directly from the icterus, the quantity thus disposed of is very large. True, there occurs in this form of icterus a condition not met with in any other kind of mechanical jaundice, namely a *crystalline* deposit of bile-pigment in the urinary tubes, in the form of most beautiful rhombic prisms and needles of bilirubin. So enormous may be the quantity of these bilirubin crystals in fatal cases, that the whole of the tubules of the pyramids are actually stuffed full of them, giving rise to a perfect "*bilirubin-infarct.*" These infarcts are larger than the uric acid form, and are only distinguished macroscopically from the latter by their intense golden hue. In the pelvis of the kidney I have also repeatedly observed enormous quantities of large bilirubin crystals; at the same time the tubes of the cortex, while containing diffusely golden coloured cylinders, presented only extremely minute bilirubin crystals, though these were present, it is true, in large numbers. With such a condition of the kidneys, crystals of bilirubin are invariably found in the interior of the vessels, and the buffy clots are usually so rich in them as to acquire a saturated orange colour. There is no more doubt, however, that the latter appearance is due to a post-mortem formation of crystals than there is of the ante-mortem origin of the crystalline deposits in the interior of the urinary tubules. Why the biliary colouring matter of the new-born has this marked tendency—not observed in later life—to separate out in crystalline form, I am quite unable to say. For the rest, the excretion of the pigment in the urine continues as long as the jaundice lasts, *i. e.* for some time after the obstacle to the evacuation of bile is got rid of. Compared with that excreted by the kidneys, the amount of bile-pigment removed in other ways is certainly inconsiderable. The sweat-glands are the only parts whose share in excretion may be at all noteworthy.

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* Hoppe-Seyler, 'Pflüg. A.,' x, p. 208; cf. also Kunkel, 'Virch. A.,' lxxix, p. 455.

But the fate of the *bile-salts* has always excited more interest than that of the pigment. In mechanical icterus, or icterus by absorption, these salts no less certainly enter the blood than does the colouring matter; and, quite apart from theoretical reasons, we possess a very sharp criterion of this in the *decrease of the pulse-rate.* It has been shown by experiment that the slowing of the pulse is due to the action of the cholates, *in specie* of sodium cholate, whether the effect is ascribable, as Röhrig* claims, to a direct action on the ganglia of the heart, or, as Löwitt[*] argues, to an action on the vagus centre. If no pyrexia complicates the mechanical icterus a slowing of the pulse is never absent, and may sometimes be very pronounced. Again, the absorption of the bile-acids is proved by their presence in the urine, evidence of which was first offered by Hoppe[†] and Kühne,[‡] and which has been repeatedly confirmed by numerous later writers. But though the fact that bile-acids can be detected in the urine in every mechanical icterus is established beyond dispute, it is no less certain that their amount is *extremely slight*. What under these circumstances becomes of the other absorbed cholates? For that, as Leyden[§] attempted to show was probable, the bile-acids excreted in the urine really represent the whole amount absorbed cannot be maintained in view of the slowing of the pulse; since the contents of the blood in cholates would not then suffice for the production of this effect. Nor do we know of any part except the kidneys from which they might be excreted. There is certainly no trace of them in the intestine, as is proved by the nature of the intestinal contents and character of the motions. The only secretion in which they have been found so far is the urinary, and the sole assumption of the kind remaining open is, that a portion of the bile-acids absorbed is again given up by the liver-cells to the bile-capillaries. But no such strange hypothesis is required, I think; a more natural conclusion, in my opinion, is that the bile-acids are distributed from the blood throughout the whole of the exudations and juices, and that the portion which is not excreted by the kidneys is there decomposed and destroyed. This assumption, which is the most plausible of all when considered with reference to the fate of bile-acids under physiological conditions, is the only one that harmonizes with the fact that icterus by absorption may, as a rule, continue for many weeks and months, without seriously endangering the patient's constitution. For we know that the cholates are very far from harmless, but possess in a marked degree the inherent capacity of *dissolving the blood-*

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* Röhrig, 'A. d. Heilk.,' iv, p. 385.

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[*] Löwitt, '(Prager) Zeitschr. f. Heilkunde,' ii, p. 459.

[†] Hoppe, 'Virch. A.,' xiii, p. 101.

[‡] Kühne, 'Virch. A.,' xiv, p. 310.

[§] Leyden, 'Pathologie des Icterus,' p. 39.

corpuscles; and if a considerable accumulation of bile-acids took place in icterus this would be for the blood a really fatal occurrence. I am very far, however, from wishing to deny the possibility that some of the blood-corpuscles are actually dissolved by the bile-acids absorbed in jaundice, but the number cannot be large, as the passage of free hæmoglobin into the transudations and urine would certainly betray it. While it is, therefore, established that no great accumulation of cholates takes place in ordinary icterus in the blood, the fact that the remaining symptoms, in the great majority of cases, are scarcely more than a feeling of indisposition and languor, with a bitter taste in the mouth and itching of the skin, speaks unmistakably for the view that, in the juices of the parenchyma also, the entrance of the cholates is rapidly followed by their destruction.

But if these symptoms, called forth by the absorption of the biliary constituents, be added to the severe digestive disturbance occasioned by the absence of bile from the intestine, you will agree with me in pronouncing every absorption icterus of some duration to be a really serious affection. Still the icterus will very frequently be borne fairly well for months or even years; in the very decided majority of autopsies, it is not the jaundice itself but some complication or other that is found to have caused death, or this may be the result of the disease giving rise to the icterus, as *e.g.* carcinoma of the bile-duct or duodenum. Nor is it by any means a rare experience that persons who have been intensely jaundiced for many months recover completely and regain their former state of health, when the stone which had obstructed the duct fortunately slips into the duodenum. Still you must not always count upon so comparatively favorable a course in mechanical icterus. It sometimes happens that when the affection has for a long time run a perfectly typical course, much more threatening symptoms are suddenly developed, producing the clinical picture which by contrast with ordinary jaundice has for ages been termed *icterus gravis.* If, in the absence of pyrexial complication, the pulse of an icteric person, previously slow, experiences a considerable increase of frequency, and at the same time loses its tension and becomes easily compressible, this alone is an unfavorable sign; and the approach of dangerous symptoms is also often indicated by petechiæ, epistaxis, and bloody stools. But by far the most characteristic phenomena in icterus gravis are *disturbances of the central nervous system*. The patients become drowsy and apathetic, and this condition speedily passes on into somnolency and pronounced *coma*. As a rule, the coma is preceded by a stage of excitement with busy and noisy delirium; and even when the patients have become somnolent the coma is often interrupted by fits of raving, the *boisterous* and often really *maniacal character* of which is almost pathognomonic. More rare than such violent bursts of delirium are *convulsions*, observable in all degrees of violence from a slight general trembling to strong clonic spasms. In the end the patients cannot be aroused from the deep coma, and then, probably without exception, death ends the scene. The post-mortem appearances in these cases are also extremely characteristic, as a rule. Three series of changes strike one, mostly with equal prominence:—1, *the intensely icteric coloration* of the tissues, in connection with the absence of bile from the intestine; 2, small and large hæmorrhages into all parts of the body, the subcutaneous fat and the mediastinum, the epi- and endo-cardium, the lungs, the gastro-intestinal canal, the omentum, the meninges of the brain, the pelves of the kidneys, &c; and 3, an extreme degree of *fatty change*, at least in the heart, the kidneys, and the liver, and sometimes in addition of the voluntary muscles, though here it is less marked. In the liver the appearances are not always limited to a combination of icterus with fatty change. When the escape of bile has long been obstructed, a more or less extensive increase of the *interstitial connective tissue* of the organ is occasionally found—a condition which led Charcot* to distinguish a special form, *cirrhose biliaire*, from the ordinary cirrhosis. True, I do not agree as to the applicability of the view that this interstitial hepatitis is set up by the irritating qualities of the stagnant bile, fitting it to act as an exciter of inflammation, or by an inflammation of the bile-ducts starting from the ductus choledochus and extending into the liver. The slowly and gradually increasing ectasis of the bile-ducts, as the result of occlusion of the ductus choledochus, must, when fairly well marked, necessarily cause atrophy or even destruction of the hepatic cells forming the peripheral zones of the lobules; and, just as in all other parts, the disappearance of the parenchyma is followed by an increase of the interstitial connective tissue. Moreover Beloussow* has shown that in biliary stagnation, more especially when rapidly developed, there take place numerous small ruptures of the minute bile-ducts, which themselves give rise to circumscribed necrotic foci in the hepatic tissue, also followed by consecutive inflammatory formation of connective tissue. The intensity of these last-named changes—the destruction of the liver-cells and the secondary cirrhosis—may vary extremely, being at one time very considerable, at another scarcely perceptible.

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* Charcot et Gombault, 'Arch. de phys. normale et pathol.,' 1876, p. 272, 453; Du Costel, 'Arch. génér.,' 1876, Sept.; J. Wickham Legg, 'Lancet,' 1877, ii, No. 6; Ackermann, 'Virch. A.,' lxxx, p. 396.

It is this variable character that, in my opinion, forbids us to make the icterus gravis depend upon the disappearance of the hepatic cells. And those writers also who regard the symptoms above described as the expression of an "acholia" have not had this kind of destructive process in mind, but a much more extensive disappearance of the hepatic parenchyma. Now it would certainly be theoretically conceivable that the interlobular veins may be so compressed by the ectatic bile-ducts that the capillary circulation of the lobules, and by consequence the nutrition of the hepatic cells, are reduced to a quite inadequate standard; and following out this idea the hæmorrhages from the stomach and intestine have been attributed to mechanical hyperæmia. Still we may decline to discuss this possibility simply because in a decided majority of the cases of icterus gravis *the hepatic cells are thoroughly well preserved.* The only alterations displayed by them are *pigmentation* and *fatty change;* and the assumption that the cells containing the pigment and fat no longer perform their functions, and in particular produce no bile, has, so far as I see, no grounds to support it. No less inadequate is the explanation of Leyden,† who attributes the grave symptoms of the icterus to a true *cholæmia, i. e.* an *overloading of the blood with cholates*, which itself is supposed to depend on *a falling off in their excretion by the kidneys.* For, in the first place, a diminution of the urinary secretion is very far from a constant symptom of icterus gravis; and, in the second place, the quantity of bile-acids excreted with the urine in mechanical icterus is much too trifling in comparison with the total amount absorbed, for their non-excretion to be followed by such serious consequences: the organism, which can dispose of so much larger quantities of cholates, would have the power of destroying this trifling increase also. From the standpoint just taken up by us, it is obvious that an overloading of the blood with bile-salts, an actual cholæmia, could at most result from the further incapacity of the organism to decompose and render innocuous the salts absorbed. But who can say whether the living organism can ever lose this capacity?

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* Beloussow, 'A. f. experiment. Pathol.,' xiv, p. 200.

† Leyden, loc. cit., p. 180 *et seq.*

It would at any rate be very desirable to explain, if possible, the symptoms of icterus gravis, without having recourse to an hypothesis such as this, which so far is incapable of proof. And I believe it to be possible. For on analysing the complex of clinical symptoms and anatomical appearances which together make up the picture of disease now under discussion, it is evident that the icteric coloration, usually so intense throughout the entire body, requires no special elucidation. With two of the remaining symptoms we are already familiar, namely, the hæmorrhages and the fatty changes. The hæmorrhages have quite a scorbutic character; and without wishing now to decide whether they occur by rhexis or by diapedesis, *i. e.* whether they depend on increased lacerability or on increased permeability of the vessel-walls (cf. vol. i, p. 396), we need not hesitate to declare that they are the manifestation of *the effect exerted by the defective constitution of the blood on the nutrition of the vessel-walls.* As regards the fatty changes, you know from former discussions that they are mainly attributable to *abnormally increased disintegration of albumen.* The cause of this disintegration has already been hinted at; it is chiefly the absence of bile from the intestines. As formerly stated, an individual in whom the absorption of food-fat is reduced in the extreme, must, in order to support life, secure the necessary supply of fat by separating it from albumen. But for this, enormous quantities of albumen would be necessary, more even, in long-continued stoppage of bile, than the digestive organs can provide, especially when the pancreas is at the same time crippled. The inevitable result of this will be a call upon, and splitting up of, the albumen of the body itself. In addition there occurs a solution of some of the blood-corpuscles, which, though moderate in amount, is continuous, and the importance of which is here intensified by the difficulty of replacing the corpuscles owing to the defective nutrition. And there is also the injury to the heart and its ganglia which persists during the entire affection, and expresses itself at first only by a slowing of the pulse-rate, but usually after a time by a lowering of arterial pressure. If there be a disease which must necessarily lead to impairment of the composition of the blood as well as to imperfect nutrition of the body and the organs composing it, this disease is long-persisting mechanical icterus. And this being so, the severe *cerebral disturbances* are, I believe, explainable without any need for supposing a specific poisonous action of the bile-acids, though such action is not impossible.* For, as Traube† many years ago declared, the cerebral symptoms in the so-called cholæmic are not essentially to be distinguished from the similar disturbances so often observed towards the end or after the crisis of acute diseases which have run a rapid course; they have the characters of so-called *delirium of inanition*, or of anæmic convulsions. Accordingly, the fundamental conditions necessary to the development of icterus gravis are really presented by every long-standing mechanical jaundice; yet for its actual development a number of special circumstances must coincide. Above all, it cannot possibly make its appearance so long as the loss of fat can be compensated by the digestion; and, further, its occurrence is decidedly favoured by the somewhat *sudden* failure of the compensatory digestive action. Where it is not sudden, a rapid deterioration of the blood attended by the consequences already described does not ensue. The body then falls a gradual prey to the slowly progressive marasmus, and to this the patient, extremely emaciated and reduced, finally succumbs.

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* Löwitt, (Prager) 'Zeitschr. f. Heilkunde, ii, p. 459.

† Traube, 'Gesammelte Abhandl.,' ii, p. 815.

But if the view just explained be correct, and we may regard icterus gravis, not as a specific picture of disease, but as the expression of *a deterioration of the blood, with inanition—chiefly brought about by an abnormally abundant disintegration of the albumen of the body,—and accompanied by extreme jaundice;* then the entire complex of symptoms, except the icterus, must also occur under other circumstances, provided an abnormally increased disintegration of the albumen of the body is initiated by some agency or other. Here I may remind you of *acute phosphorus-poisoning*, in which the urine bears the most striking testimony to the extreme increase of albuminous waste (vol. ii, p. 671). In it you find precisely the same fatty changes, the same hæmorrhages, the same easily compressible pulse, the same prostration and somnolence; and if the maniacal delirium is absent as a rule, it is well to consider whether the phosphorus does not exert a specially depressing action on the functions of the brain. At any rate, the typical *so-called cholæmic seizures* are not absent in another disease, which, greatly to our disadvantage in understanding it, has repeatedly been confounded with icterus gravis—I refer to *acute hepatic atrophy*. Here everything corresponds with what is seen in icterus gravis, the hæmorrhages, the fatty changes, the pulse, the cerebral disturbances, everything—except the complete occlusion of the bile-passages. In this disease, consequently, jaundice may not occur, or if present, will always be very slight, like that observed in simple catarrhal icterus; the contents of the bowels, also, are never quite uncoloured. This being so, the extreme increase of albuminous waste cannot be referred to a want of bile in the intestine; while the occurrence of such waste is clearly evidenced by the urine. It must be quite another cause, though at present unknown, that in this disease gives rise to those profound changes in the metabolism of the body which in icterus gravis are brought about by long-continued absence of bile from the intestine. But whether the unknown agent exerts its destructive influence in the first instance on the liver, and by its action on this organ initiates the increased albuminous waste, or whether the degeneration of the liver is only a part-phenomenon or a consequence of the profound derangement of metabolism, cannot, as recently stated (vol. iii, p. 891), be decided in the present state of our knowledge. Still the fact that atrophy of the liver* is developed in somewhat chronic phosphorus-poisoning also, in some measure tells in favour of the second alternative.

Despite the many evident imperfections in our knowledge of icterus, the subject is one with which we are well acquainted as compared with the second side of the liver's activity, the *production of glycogen*. Not that we here enter a little explored province. On the contrary, there is scarcely another subject in physiological chemistry which, during the two decades that have elapsed since the discovery of hepatic glycogen by Bernard and Hensen, has attracted such a host of scientific workers. These experimenters have been drawn no less from the ranks of pathologists than of physiologists, because nowhere else do pathology and physiology so intimately touch. We are, moreover, in possession of a number of well-established facts with regard to it. We know that the glycogen is contained in masses in the interior of hepatic cells, irregularly distributed throughout the lobules, and that it can be rendered recognisable under the microscope by means of Lugol's solution.† We are, further, fairly well informed as to the conditions on which its presence in the liver depends. *Food* is undoubtedly the chief factor influencing it—a fact confirmed by all writers since Bernard's first observations. Thus, in prolonged starvation, the glycogen completely disappears from the liver of rabbits, dogs, guinea-pigs, hens, pigeons, &c.; and, on the other hand, accumulates most abundantly when the animals' diet consists of a plentiful supply of mixed albuminous substances and carbohydrates. A very energetic discussion has quite recently been carried on with regard to the intimate relations, the theory, if you will, of this production of glycogen. Very much as we found when discussing the formation of fat, so here it has been inferred that because the introduction of sugar into the intestines, or better into a tributary of the portal vein, in starving animals, is quickly followed by the appearance of glycogen in the liver, the glycogen is produced from the sugar by the formation of an anhydride. Yet though the fact itself is indisputable, it has been shown by Forster[*] that the quantity of glycogen produced under these circumstances is not even approximately equal to the amount of sugar introduced, but forms an insignificant fraction of it. Moreover, according to Wolffberg,[†] when the amount of sugar given remains the same, and is accompanied by the administration of increasing quantities of dried and pulverised flesh, the glycogen contained in the liver becomes proportionately augmented. Further, Naunyn,[‡] Wolffberg, v. Mering,[§] and others have more recently observed an accumulation of glycogen in the liver after an albuminous diet, completely free from carbohydrates. Lastly, the liver in hybernating animals contains considerable quantities of glycogen, although the animals do not consume a particle of carbohydrates for months together.[‖] In view of these facts, the question, in my opinion, is not whether carbohydrates *or* albuminous bodies are the antecedents of the glycogen; we can at most discuss the possibility *that besides albumen other glycogen-builders exist.* It appears to me, too, that in putting the question, no sufficiently sharp distinction has been drawn between the *production* and the *accumulation* of glycogen. For, as Wolffberg justly remarks, we cannot in the least infer how much glycogen is produced, from the amount present in the liver. The case exactly resembles that of fat and the other decomposable constituents of the body; everything depends on the amount of *consumption taking place coincidently.* A large quantity of glycogen may be formed in the liver, and yet, if there be a corresponding destruction, very little will be present in the organ; while if there be no destruction, a very trifling production may lead to a very considerable accumulation. The manufacture of glycogen is evidently a continuous function of the liver-cells, which, like all other functions, may vary in intensity, and will certainly be most energetic when the body is well nourished. But that it is not extinguished during fasting is proved by the livers of hybernating animals; in them, owing probably to the absence of muscular movements,* the glycogen accumulates undecomposed, while in an ordinary condition the consumption keeps pace with the production. The carbohydrates, then, do not form glycogen, but *preserve* it; at least they are engaged in its formation only in so far as their consumption augments the disintegration of albumen: their main office is to preserve the glycogen, the easily decomposable sugar protecting the latter against further chemical change. To the importance which attaches to the poverty of the blood of the hepatic capillaries in oxygen, as allowing the accumulation of glycogen in the liver, your attention has already been repeatedly drawn.

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* Cf. Fraenkel, 'Berl. klin. Wochenschr.,' 1878, No. 19; Erman, 'Vierteljahrschr. f. gerichtl. Medicin,' N. F. xxxiii, p. 61.

† Bock und Hoffmann, 'Virch. A.,' lvi, p. 201.' The quantitative distribution of the glycogen in the liver appears to be approximately equal throughout, so that Seegen and Kratschmer ('Pflüg. A.,' xxii, p. 214) regard the organ, from this point of view, as a unit.

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[*] J. Forster, 'Sitzungsber. d. bayr. Akad. d. Wissensch.,' 1876, p. 138.

[†] Wolffberg, 'Zeitschr. f. Biol.,' xiv, p. 266.

[‡] Naunyn, 'Arch. f. experim. Pathol.,' iii, p. 85, *et seq.*

[§] v. Mering, 'Pflüg. Arch.,' xiv, p. 274.

[‖] Schiff, 'Untersuchungen über d. Zuckerbild. in d. Leber,' p. 30. Aeby, 'Arch. f. experim. Pathol.,' iii, p. 180; Voit, 'Zeitschr. f. Biol.,' xiv, p. 112, *et seq.;* Külz ('Pflüg. A.,' xxiv, p. 74) is, it is true, inclined to regard the quantity found in hybernating animals as the remains of the glycogen accumulated by the animals at the beginning of their sleep.

The capacity of *producing* glycogen is obviously dependent on the integrity and normal constitution of the hepatic cells. It need hardly be said, therefore, that an abnormally small amount will be formed when a great part of the hepatic parenchyma is compressed by tumours or by echinococci, or has been obliterated or destroyed by suppuration, amyloid degeneration, or some atrophic process. This also applies to extreme *fatty liver*, in which the fat has originated at the expense of the albumen; thus, Saikowsky† has determined the entire absence of glycogen from livers which were fattily degenerated as the result of phosphorus- or arsenic-poisoning. In such investigations, however, it is necessary to bear in mind that the amount present in the liver will be very greatly influenced by the nutritive condition of the animal. Hence Bernard's emphatic statement that a great abundance of glycogen cannot be counted on in the livers of animals which are from any cause diseased; while as for the fact established by Manassein,* that in the *pyrexia* of animals the hepatic glycogen undergoes a marked diminution, and may even disappear, it would be hard to decide in how far this result should be referred to the defective state of nutrition of the diseased animals. One might almost be tempted to take up a similar position with regard to the disappearance of glycogen which several observers† have determined to occur after *ligature of the ductus choledochus;* yet the falling off in the glycogen-contents of the liver here follows too rapidly to allow of our excluding the exertion by the operation of a specific influence on the glycogen-forming or perhaps glycogen-destroying capabilities of the hepatic cells.

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* Voit, loc. cit.; cf. also Külz, 'Pflüg. A.,' xxiv, p. 41.

† Saikowsky, 'Virch. A.,' xxxiv, p. 73, 'Med. Centralbl.,' 1865, p. 769.

Our real difficulty begins, however, only when we attempt to come to a conclusion as to the importance for the organism of the variations in the amount of glycogen produced and stored up in the liver. As the result of a large number of extremely accurate investigations, it is now certain that *sugar is a regular and constant constituent of the blood-serum*, and that even after long starvation and in exhausting diseases it is present in it in scarcely diminished quantities, and never completely disappears during life. But this by no means implies that the hepatic glycogen has anything to do with the sugar-contents of the blood. The fact that a formation of sugar invariably takes place at the expense of the glycogen in a liver removed from an animal, naturally from the first suggested the idea of a constant conversion during life also, by the aid of a ferment present in the liver. The objection taken to this assumption, that when the liver is manipulated with all possible speed, at most only traces of sugar are detectable in it, has, it is obvious, no serious importance, inasmuch as the new-formed sugar may at once be carried off by the blood. Yet, although the possibility of this transformation of hepatic glycogen into sugar will not be disputed, the evidence brought forward by Bernard in proof of it is now very far from incontrovertible. Bernard, as is well known, based his view on the alleged fact that the blood of the arteries contains more sugar than does that of the veins of the extremities, so that between the periphery and the heart there must be situated an apparatus by which sugar is produced. He attached still greater importance to comparative analyses of the blood contained in the portal and hepatic veins. Except during digestion, he found the portal blood free from sugar, but could always detect its presence in the blood of the hepatic vein. None of these results have been confirmed by the most recent writers, working with improved methods. Abeles,* v. Mering,† and others found, on the contrary, that while the amount of sugar in the blood varies within certain limits, there are no noteworthy, or at all constant, differences in the sugar-contents of the different vessels. In particular they not only did not fail to detect sugar in the portal vein, but discovered that its amount in fasting animals is the same as that of the blood in the carotid. More than this; during the digestion of amylaceous matters and sugar, v. Mering found the blood of the portal to contain considerably more than that of the hepatic vein. Even the statement of Bock and Hoffmann,‡ that the blood loses its sugar in forty-five minutes after the liver is cut off from the circulation, has not been confirmed by Abeles;§ and even if the occurrence were established, the conclusions to be drawn from it would be open to doubt on account of the severity of the operative procedure. But since even after long starvation the amount of sugar in the blood is scarcely diminished, while only traces of glycogen remain in the liver, Abeles seems to me to be correct in concluding that *analyses of the blood do not, so far, justify us in regarding the liver and its glycogen-contents as a source of the sugar normally present in the blood.* Unfortunately, too, we are not in a position to replace Bernard's theory by a better established one. There is no doubt of course that the glycogen produced and stored up in the liver disappears from it and is finally burnt into carbonic acid and water. We also know from Külz that forced and prolonged muscular exertion,* as well as marked reduction of an animal's temperature,† greatly accelerates the decomposition of glycogen. But the details of the decomposition are still completely hidden; we know nothing of the intermediate and preliminary stages of the oxidation; and although, obviously, it cannot for a moment be supposed that the glycogen is transported in substance from the liver to other parts, *e. g.* the muscles, we are unacquainted even with the localities in which it undergoes its successive changes.

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* Manassein, 'Virch. A.,' lvi, p. 220.

† J. Wickham Legg, 'Brit. Med. Journ.,' 1876, 268; 'A. f. exp. Path.,' ii, p. 384; v. Wittich, 'Med. Centralbl.,' 1875, p. 113, 291; Külz und Frerichs, 'Pflüg. A.,' xiii, p. 460.

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* Abeles, 'Wien. med. Jahrb.,' 1875, Hft. 3.

† v. Mering, 'A. f. Anat. u. Physiol.,' 1877, Phys. Abth., p. 379, contains references to literature

‡ Bock und Hoffmann, 'Experimentalstudien über Diabetes,' Berlin, 1874.

§ Abeles, 'Wien. med. Jahrb.,' 1875, Hft. 3.

But ought we to rest content for the present with these perfectly negative results? Should we not rather bear in mind the inadequacy, more than once expressed, of all conclusions based on comparative analyses of the blood? There are, in truth, certain facts which, despite all that has preceded, speak in a most unmistakable way for the existence of intimate relations between the hepatic glycogen and the sugar of the blood. I have now in mind that process on which is concentrated the main interest of the entire glycogen-question for the pathologist, namely *artificial diabetes mellitus.* We speak, you are aware, of diabetes mellitus when the urine contains an amount of grape-sugar that may be recognised by its rotating the plane of polarisation to the right, by Trommer's test, and by fermentation. Normal urine also contains, it is true, at all times a quantity of sugar—a fact first proved by Brücke, since often disputed, and again and again confirmed by other writers.‡ But the amount normally present is too small to allow of our ever obtaining the characteristic reactions except by adopting a complicated special preparatory process. This poverty of the normal urine in sugar corresponds with the insignificant amount contained in normal blood; only when the blood becomes richer in sugar does a larger quantity pass over into the urine. The normal amount of sugar in the blood does not usually reach and rarely exceeds 0·1 per cent., though it varies a little with the species and also among different members of the same species. The following amounts *pro mille* have been determined :—Pavy[*] found on the average in dogs' blood 0·787, sheep's blood 0·521, ox-blood 0·543 ; Abeles,[†] on the average in dogs 0·5 ; Bock and Hoffmann[‡] in rabbits 0·7—1·1 ; in cats, Böhm and Hoffmann[§] obtained a somewhat higher mean, 1·5 ; v. Mering[||] determined the sugar-contents of the blood-serum of dogs to be between 1·1 and 2·3, and, in serum obtained by venæsection from two persons suffering from pneumonia, he found respectively 1·2 and 1·3 of sugar. Corresponding with this, there is also a variation, within certain limits, of the value that must be attained by the sugar-contents of the blood before sugar can be excreted with the urine in easily detectable quantities : for the dog, according to Bernard, these limits are 2·5—3 *pro mille*, in rabbits somewhat higher. Diabetes simply implies, accordingly, *an abnormal increase of the sugar of the blood*, and in seeking to explain the disease, the problem requiring solution is, the causes of the richness of the blood in sugar.

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* Külz, 'Pflüg. A.,' xxiv, p. 41.

† Ibid., p. 46.

‡ Its most recent confirmation is the paper of Abeles, 'Med. Centrlbl.,' 1879, p. 33.

Now—quite independently of the direct injection of a solution of grape-sugar into the vascular system—we are acquainted with a very great number of methods by which rabbits, dogs, cats, frogs, and other animals may in a short time be rendered diabetic. If we cause the animals to inhale carbonic oxide or amyl nitrite, or narcotise them with ether, morphia, or chloral hydrate, or administer a poisonous dose of strychnine, corrosive sublimate, turpentine, or of any of a number of other substances,[¶] we may be prepared to find a more or less marked glycosuria. Even after the introduction of large quantities of a weak salt-solution into the vascular system, rabbits and also dogs become diabetic.[**] As the result of various disturbances of the *nervous system*, the urine may also contain sugar. Cats, in particular, in whose blood, it is true, a comparatively large amount of sugar is normally present, become diabetic after all possible kinds of injury; the securing of the animals on the operation table suffices to produce it, especially when at the same time tracheotomy is performed.* With regard to diabetes produced by injury to the brain and spinal cord, as well as to the sympathetic and its ganglia, there already exists a very extensive literature.† Of all the methods adopted, none probably is more celebrated or more often employed than Bernard's *piquûre*, and next to this, the *curare-diabetes*, also discovered by Bernard. The former consists, as is well known, in puncturing the floor of the fourth ventricle; while the poisoning with curare may be so graduated that all the voluntary muscles except the respiratory shall be paralysed, or the animal's respiration may be maintained artificially; but as regards the success of the glycosuria the choice is of no importance. Shortly after the puncture or the occurrence of paralysis, the sugar-contents of the blood increases to double or treble the normal, and it is not long till the urine passed or drawn off from the bladder yields with Trommer's test a marked precipitate of yellow or red cuprous oxide. The first sugar usually appears in the urine in from thirty to forty minutes after the infliction of the puncture or administration of the poison; from that time forwards its excretion rapidly increases, till after about an hour it reaches its maximum, and then gradually diminishes and finally disappears. The excretion is frequently, but by no means always, associated with pronounced polyuria. In rabbits, the diabetes lasts not more than from five to six hours, except in very exceptional cases; in dogs, Bernard had never observed it for more than twenty-four hours. A perfectly similar course was run, according to Naunyn,‡ by diabetes produced by carbonic oxide, and, according to Böhm and Hoffmann,§ by that developed in cats by securing them on the operation table; so that these events are probably characteristic of all forms of artificial glycosuria.

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[*] Pavy, 'Med. Centrlbl.,' 1877, p. 630.

[†] Abeles, 'Wien. med. Jahrb.,' 1875, Hft. 3.

[‡] Bock und Hoffmann, 'Experimentalstudien über Diabetes,' Berlin, 1874.

[§] Böhm und Hoffmann, 'A. f. experim. Path.,' viii, p. 271.

[||] v. Mering, 'A. f. Anat. u. Physiol.,' 1877, Phys. Abth., p. 379. Contains references to literature.

[¶] Cf. Senator's statements on this point, 'Ziemssen's Handb.,' xiii, i, p. 481, *et seq.*

[**] Bock und Hoffmann, 'A. f. Anat. und Phys.,' 1871, p. 550.

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* Böhm und Hoffmann, 'A. f. experim. Path.,' viii, p. 271.

† Cf. especially Eckhard, 'Beiträge z. Anat. und Physiol.,' iv, 1867; vi, 1872; viii, 1877. Cf. further Külz, 'Pflüg. A.,' xxiv, p. 97.

‡ Naunyn, 'Arch. f. experim. Pathol.,' iii, p. 85, *et seq.*

§ Böhm und Hoffmann, 'A. f. experim. Path.,' viii, p. 271.

But what has this artificial diabetes to do with the liver and its glycogen? It fails to set in after puncture or curare-poisoning in frogs *from which the liver has been extirpated;* and if already established from either of these causes, it rapidly disappears on removal of the organ.* In rabbits the occurrence of artificial diabetes may be prevented by excluding the liver from the circulation; yet these animals survive the operation only a short time, and its severity is in any case such as to make another method of proof desirable. As a matter of fact, *the absence of glycogen from the liver* is in itself enough to render the most approved methods of producing diabetes ineffectual. Animals cannot be rendered diabetic by means of the *piqûre,* or by poisoning with curare or carbonic oxide, if they have been long starved or their livers deprived of glycogen† as the result of phosphorus- or arsenic-poisoning. These facts have not, it is true, the same value as a pure experiment; for protracted hunger does not simply cause the glycogen to disappear from the liver alone, and whether the phosphorus and arsenic do not also bring about the removal of the glycogen of the muscles still needs to be investigated. For these reasons, the fact ascertained by Wickham Legg‡ appears to me to carry more conviction with it. This writer found that the puncture is rendered non-effective by previous ligature of the ductus choledochus; and it would obviously be forced to attribute this effect of the trifling operation to anything but the liver, from which the glycogen, as already stated, disappears in consequence of the ligature.

But though we willingly recognise an intimate connection between the liver, or its glycogen-contents, and the artificial diabetes, we must not allow ourselves to be deceived into believing that we are anything but far removed from an accurate comprehension of the nature of this connection. In order at the start to dispel a very natural error, we may say at once that we have not in artificial diabetes to deal simply with the removal of the glycogen stored in the liver and its diffusion through the blood. To say nothing of other objections, the amount of sugar excreted is much too large to have been formed from the stored glycogen of the liver; moreover, the store is not reduced by the diabetes, the usual quantity being as a rule present in the organ at the termination of the attack.* As the result of what kind of action, then, is the sugar of the blood increased till it amounts to actual diabetes, in consequence of procedures so different in their nature? In truth, it might appear difficult enough to discover any common feature between the puncture, the curare-poisoning, the binding on the table, &c., upon which a line of reasoning might be based. The attempt has nevertheless been made, and a factor common to all these methods has been found in certain *circulatory disturbances* called forth by them; in particular, it has been assumed since Schiff's time, that the true cause of the artificial diabetes is to be sought *in a congestive hyperæmia and acceleration of the hepatic circulation.* But though I am little disposed to deny that the *piqûre*, the inhalation of amyl nitrite, the curarisation, the carbonic oxide poisoning, &c., may be followed by various circulatory disturbances, the circulation through the liver has its own especial characters. A true congestion accompanied by acceleration of the stream cannot occur in the hepatic capillaries except as the result of a decrease of resistance in the arteries which supply the tributaries of the portal with blood, *i. e.* the cœliac and the two mesenteric arteries. Such a decrease of resistance occurs during every period of digestion; the stomach and intestines are then brilliantly injected, the spleen is succulent with blood, the pancreas too is reddened during secretion, and the liver will at any rate be furnished with a much more ample and vigorous blood-supply than at other times. Yet in spite of this a healthy individual never exhibits diabetes during or after digestion, even though he has consumed large quantities of carbohydrates. Should anyone here object that the degree of physiological congestion occurring during digestion is not sufficient to produce it, he runs the danger of coming into conflict with other facts of physiology. The vascular area from which the vena portæ receives its blood is, you are aware, so roomy that an overloading of it must be attended by prejudice to the circulation generally. In herbivora more especially, and hence in the rabbit, the great decrease of resistance in the arteries of the abdomen, which follows division of the splanchnics, involves such a considerable lowering of arterial pressure that the blood-stream through the dilated intestinal vessels, instead of being accelerated, is even *retarded ;* and, conversely, after any operation on the rabbit, we may safely conclude from the unaltered mean arterial pressure that no unusual and abnormal hyperæmia of the portal area has taken place. Now, neither the puncture, nor a curarisation of medium severity, nor again the securing upon the table, is wont to influence the mean arterial pressure, and if it did so, would cause a lowering of it, which again would not involve an acceleration but a retardation of the circulation in the intestines and liver. This argument cannot be overthrown by the statements of some writers, who say that they have found the liver in diabetic animals hyperæmic at the post-mortem ; no decision can be come to even on the ground given by Bernard, that on opening the abdomen of an animal, which has been punctured or curarised, the viscera are in a state of marked hyperæmia,* especially as the opening of the abdomen and exposure of the intestines is of itself sufficient to set up a congestion of the latter. Accordingly, the assumption that artificial diabetes depends on an increased activity of the liver, or rather of its glycogenic function, brought about by an augmentation and acceleration of the portal circulation appears to me to be quite unproved. Let me be clearly understood. I do not deny the possibility that owing to the *piqûre* more glycogen is produced by the liver and at once converted into sugar ; but there is no positive proof of this, and, again, it is more than doubtful that a nervous influence on the vessels, and thereby on the flow of blood, is the determining factor in it. May not nerves be excited by the puncture that influence the activity of the hepatic cells more directly than through the medium of the vessels ? For that in the *piqûre* we are dealing with an *excitation* and not with a paralysis of nerves is rendered at least very probable by the relatively short duration of the diabetes.

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* Winogradoff, 'Virch. A.,' xxvii, p. 533.

† Saikowski, 'Virch. A.,' xxxiv, p. 73; 'Med. Centrlbl.,' 1865, p. 769.

‡ J. Wickham Legg, 'Brit. Med. Journ.,' 1876, 268; 'A. f. exp. Path. ii, p. 384.

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* Böhm und Hoffmann, 'A. f. experim. Path.,' viii, p. 271.

* Cl. Bernard, 'Vorles. über Diabetes,' Germ. Trans., p. 232.

It is possible, however, that the liver plays quite another part in artificial diabetes. I mentioned already that v. Mering's analyses went to show that, during the digestion of starches and sugar, the portal blood contains not simply an equal, but even a higher, percentage of sugar than does the blood of the hepatic vein. Should this fact prove to be generally true,[*] it appears to me to follow that part of the sugar absorbed from the intestine during digestion disappears in the liver.[†] What becomes of it is, it is true, quite unknown; I have already stated the reasons which tell against its conversion into glycogen. But however it be disposed of, it is necessary to inquire whether the richness of the blood in sugar during artificial diabetes may not partly depend on *the disappearance of a less than usual amount in the liver.* In fact, Bernard had from the first stated that the diabetes can only be produced with certainty in a healthy animal and *during the period of full digestive activity.* There are also some other facts which are well calculated to support our hypothesis. Dogs, in which Bernard had in from four to six days caused obliteration of the portal vein by means of a ligature loosely secured around it, if fed on potatoes alone, excreted an alkaline urine rich in sugar, while the same kind of food had previously given rise to no excretion of sugar in the urine.[‡] Thus it is proved that the cutting off of the greater part of the hepatic circulation alone suffices to render the blood abnormally rich in sugar, on a diet containing an abundance of amylaceous material; and we are in possession of an experiment of Seelig, communicated by Naunyn,[§] which directly teaches that in the liver of a diabetic animal less sugar is destroyed than in health. When Seelig slowly injected a solution of grape-sugar into a mesenteric vein of a diabetic starving rabbit, much more sugar was excreted in the urine that in a non-diabetic animal. It is true that he observed a similar difference when the injection was made into the jugular vein; yet the inequality was much more clearly noticeable on injecting into a tributary of the portal.

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[*] Bleile ('A. f. Physiol.,' 1879, p. 59), who employed methods similar to those of v. Mering, found in dogs that, during the digestion of sugar-forming materials, the portal blood has always a greater sugar-contents than has that of the carotid; on the other hand, he found no constant differences between the blood of portal and hepatic veins as regards the sugar contained in them.

[†] v. Mering, 'A. f. Anat. u. Physiol.,' 1877, Phys. Abth., p. 379. Contains references to literature.

[‡] Bernard, 'Vorles. über Diabetes,' p. 198.

[§] Naunyn, 'Arch. f. experim. Pathol.,' iii, p. 85, *et seq.*

As you perceive, it is not much of the proud and at one time so admired edifice of hepatic diabetes that now remains. How perfectly each link seemed to fit in that chain of facts, our knowledge of which was almost altogether due to the genius of Bernard! By means of the glycogen produced in the liver and its amylolytic ferment, this organ was believed to manufacture the sugar of the blood; and while the latter is normally trifling in amount, it would rapidly increase so soon as the activity of the liver became augmented in consequence of a more ample supply of blood. And to-day? I have sought to explain to you that our experience does not even give us an indisputable right to regard the liver as physiologically engaged in producing the sugar of the blood, that we have no certain evidence of increased activity on the part of this organ after puncture of the fourth ventricle or the administration of curare, and that an augmentation of the flow into and through the liver is very improbably a consequence of such procedures. But that which has chiefly tended to deprive the liver of its dominant place in the diabetes question was the discovery that *glycogen is widely distributed* through the organism. After Bernard himself had demonstrated its presence in many organs of the embryo, O. Nasse* recognised it as a regular constituent of muscular tissue, Hoppe-Seyler† showed its constant occurrence in living colourless blood- and lymph-corpuscles (and consequently of course in the spleen and lymphatic glands), Kühne‡ found it in the testicle of a fully grown dog, and, lastly, Schiele§ discovered it in the epithelial elements of mucous membranes which are furnished with a thick stratified epithelium. It is obvious, then, that those, too, who are ready to recognise the hepatic glycogen as an antecedent stage of the sugar of the blood, can at most refer only *a part* of the sugar to the liver. As to what share is taken by this organ, and what by the muscles and other tissues just mentioned, in the production of sugar, we have at present no means of forming an opinion. This difficulty chiefly arises, as already stated, from the fact that the quantity of glycogen accumulated at any moment affords no indication of the amount actually produced and finally converted into sugar or otherwise destroyed. It is by no means certain that the organs in which no glycogen has as yet been found do not take part in its production. Still we are somewhat better informed as to the history of muscle-glycogen. We know that the amount present in the muscles may vary greatly, not only in different individuals but in different muscles of the same individual. The richness of the muscles in glycogen does not simply depend on the food. True, it increases during digestion, and the total amount collected in the muscles some hours after an abundant meal of flesh closely approaches the quantity stored up in the liver;[*] again, it disappears during starvation, sometimes earlier, sometimes later than from the liver, but always just as completely as from the latter organ. But the richness of the muscles in glycogen is also influenced by the degree of their *functional activity*. The material is used up during contraction,[†] so that it will be most plentiful in paralysed muscles and in those which, like the muscles of the breast in hens, have little work to do.[‡] The fate of the glycogen used up is by no means accurately determined, more especially as Böhm[§] has demonstrated the untenability of the view that it gives rise to lactic acid before breaking up into its final products. Such being the position of affairs, it will not occur to anyone to estimate the amount of glycogen produced from the quantity present in the muscles at any time; but does our ignorance of the conditions on which the destruction of glycogen in other organs and tissues depends, justify us in arriving at any other conclusion?

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* O. Nasse, 'Pflüg. A.,' ii, p. 97.

† Hoppe-Seyler, 'Med.-chem. Untersuchungen,' Hft. iv, p. 494.

‡ Kühne, 'Virch. A.,' xxxii, p. 535.

§ Schiele, 'Das Glykogen in normalen u. patholog. Epithelien,' I.-D Bern, 1880.

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[*] Böhm, 'Pflüg. A.,' xxiii, p. 44.

[†] O. Nasse, 'Pflüg. A.,' ii, p. 97.

[‡] Weiss, 'Wien. akad. Sitzungsber.,' Bd. 64, Abth. 2, Juliheft; Chandelon, 'Pflüg. A.,' xiii, p. 626; Luchsinger, ibid., xviii, p. 472; Böhm und Hoffmann, loc. cit., p. 442.

[§] Bohm, 'Pflüg. A.,' xxiii, p. 44.

These considerations make it intelligible that, as already stated, the amount of sugar contained in the blood remains practically undiminished in prolonged starvation; but they must also be taken into account in discussing the genesis of true *pathological diabetes mellitus*. We may properly dispense with a discussion as to whether the experiences gained by experimental pathologists in artificial diabetes may be at once applied to typical glycosuria. For though there is a great and most important difference between them as regards duration—experimental diabetes being *a mere transitory* condition, while pathological glycosuria is *a lasting, indeed exquisitely chronic disease*,—yet the proximate and immediate cause of the excretion of *sugar* is the same in both, namely the *abnormally large amount contained in the blood*. A great deal of evidence may be produced to show how much this latter factor influences the whole of the phenomena of diabetes. To the abnormal richness of the blood in sugar, I attribute its excess in the lymph and transudations, its passage into some of the secretions, as, for example, the sweat, bronchial mucus, bile, occasionally the gastric juice, the saliva, &c.;* again, the imperfect constitution and reduced resisting power of the vessel-walls, on which, as formerly stated (vol. i, p. 338; vol. ii, p. 561), depends the tendency of the diabetic to severe inflammation, more especially of the necrosive form; lastly, and chiefly, the two symptoms by which a suspicion as to the existence of diabetes is usually first aroused, I mean the enormously increased *thirst* and the *polyuria*. That the latter two conditions are closely connected and stand in a direct relationship of dependence to the glycæmia cannot be doubted; the only question is as to the nature of this relationship. It has been formulated as follows:—The excretion of sugar is aided by the passage of considerable quantities of water through the glomeruli; this water is withdrawn from the blood; and the concentrated blood excites the sensation of thirst. But while it will not be disputed that the excretion of sugar involves the simultaneous passage of water into the urinary tubules, the quantity of water got rid of by a diabetic person is much greater than would be required for this purpose; and above all the incorrectness of the interpretation is shown by the fact that the sugar- and water-contents of the urine are very far from running parallel even in the same individual. It is not because the diabetic patient urinates copiously that he drinks large quantities of water; on the contrary, *he passes a large amount of urine because he drinks excessively*. And it has also been shown in an exact manner by Külz,[*] as against doubts expressed by others,[†] that the expenditure of water in diabetes is more than covered by the water consumed, provided the watery contents of the solid food be taken into account, so that the percentage falling even on the insensible perspiration is far from being always small. Accordingly, the thirst is called forth by the abundance of sugar in the blood, and only because it is satisfied is there an increased excretion of water. But whether the thirst is due solely to the *concentration* of the blood or the juices of the parenchyma, or whether the sugar exerts a specific influence on the nerve-terminations in the mucous membrane of the palate and pharynx, cannot at present be determined.

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* For a fuller statement vide Külz, 'Beiträge,' ii, p. 129.

While, therefore, our main object in human diabetes also must be to explain the glycæmia, I need not say at this stage of our inquiry that we have not to deal with the appearance of a foreign substance, not occurring in normal blood, but simply with the *quantitative increase* of a material normally present in it. The blood of healthy persons contains sugar, usually, it is true, in the small proportions already given; yet there are cases in which the amount is permanently slightly in excess, but without prejudice to health. The sugar of the blood is derived from two sources. We are constantly supplying it to the blood from the intestine by the amylaceous constituents of our food; but since the sugar-contents of the blood are not diminished by a diet perfectly free from carbohydrates, it necesarily follows that the organism is endowed with a capacity for producing sugar from albumen, probably by forming glycogen in the first instance, and the conversion of this into sugar. But if, in spite of this continuous supply to the blood, its contained sugar does not in a healthy individual exceed the known mean standard, this is only possible because the increased supply is normally accompanied by an increased consumption. In fact, the healthy organism is capable of appropriating very considerable quantities of sugar to its purposes, *i. e.* of decomposing it; and very large amounts of bread and other farinaceous food may be taken in health without any risk of the urine containing sugar. There are, however, certain limits to this. A man or a dog which consumes very great quantities of sugar, say 100, 200, or more grams, *in a very short time*, usually excretes a not inconsiderable portion of it with the urine passed during the next few hours—an evident indication that a temporary overloading of the blood has taken place in consequence of the consumption for organic purposes failing to keep pace with the rapid and abundant supply. Now every true diabetic person is distinguished from the healthy individual by this—*that even after partaking of moderate quantities of carbohydrates* (which would be completely consumed in health), *sugar is excreted in the urine.* This is the essential and decisive criterion of diabetes, one which is always employed in practice where the suspicion of the disease is to be verified. The above-mentioned individuals, whose blood constantly contains an excess of sugar, have very usually a small amount in the urine capable of being detected directly by Trommer's test; they are not, however, diabetic, since the sugar in the urine is not increased by an amylaceous diet. And, on the contrary, a person may be distinctly diabetic without the urine giving the least reaction to the ordinary tests for sugar—provided his diet is an appropriate one, *i. e.* free from carbohydrates. Since M. Traube first called attention to this fact in an important paper,* many authors distinguish two forms of the disease, a *mild* and a *severe*, while admitting that one may pass into the other. The mild form is characterised by the fact that the urine does not contain sugar except when the diet includes sugar or starch, while in the severe form sugar is excreted when carbohydrates are altogether abstained from, *i. e.* on a purely meat diet. I am not at all disposed to question the justice of such a distinction; on the contrary, it appears a very desirable one from a practical point of view. For if it be correct that, as already stated, most of the symptoms of diabetes, and those the most striking and troublesome, depend on the excess of sugar in the blood, it is evidently of the greatest importance to the patient that he has the power of voluntarily controlling this excess. Though the fundamental diseased condition continues unaltered, such a diabetic patient may enjoy a state of well-being simply by adopting a suitable dietary, while one who suffers from the severe form can never be quite free from the symptoms of his disease. But when the question is raised whether, in the two forms, we are dealing with processes differing in principle, our answer must, in my opinion, be *decidedly in the negative.* For on translating the notion of glycosuria into glykæmia, or more correctly, *hyperglykæmia,* it at once appears that only quantitative differences can be involved. In the severe form of diabetes the sugar manufactured by the organism suffices to render the blood hyperglykæmic, while in the mild form this condition is not developed till an additional quantity of sugar is supplied to the blood with the nutriment. Nor is there any necessity for assuming that the direct mode of origin of the hyperglykæmia differs in the two cases. As regards this point, it is theoretically equally conceivable that the disease is the result of an *abnormally increased production of sugar by the organism,* or the expression and effect of the *incapacity of the body to use up and destroy the sugar of the blood in the normal fashion;* lastly, it is possible that *both may concur.*

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[*] Külz, ibid., i, p. 31, *et seq.*

[†] Gäthgens, 'Ueb. den Stoffwechsel eines Diabetikers verglichen mit dem eines Gesunden,' Inaug.-Dissert., Dorpat, 1876; cf. also H. Oppenheim, 'Pflüg. A.,' xxvi, p. 259.

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* M. Traube, 'Virch. A.,' iv, p. 109.

But on seeking to decide which of these possibilities is actually concerned in a given case, we are at once met by difficulties arising out of our imperfect knowledge of the metabolism of the carbohydrates. We look in vain to *pathological anatomy* for information on this subject. No constant changes have as yet been discovered in diabetes, such as could be said to constitute the anatomical basis of the disease. Some of the appearances most frequently met with are undoubtedly consequences or complications, not causes, of the affection, as *e. g.* the general emaciation, the inflammatory and gangrenous processes in the skin, the inflammatory and ulcerative processes in the lungs, which so often simulate acute phthisis in their course, &c. As regards other conditions, only the few recorded instances of tumour of the fourth ventricle[*] could be brought into causal connection with the diabetes. On the other hand, pathologico-anatomical investigation gives absolutely negative results with respect to that organ which, following Bernard, one is accustomed to regard as having a peculiarly close connection with the disease, namely the liver. The portal vein has been occasionally found thrombosed or obliterated,[†] observations which in view of Bernard's experiments already mentioned are not without their interest; but in the enormous majority of diabetic persons the vein is perfectly free and pervious. In hospital cases—forming by far the greater number of those in which an autopsy is made—the liver as a rule contains little fat, inclines to be small rather than large, and is brown-red on section; yet we sometimes meet with large, even decidedly hypertrophic livers. The statements made as to the excess of blood in the liver after death, which one writer has copied from another, are of course valueless, even when with an eye to a naïve public it is also asserted that the hyperæmia is an active one. The pancreas[‡] is reported to be relatively often affected in diabetes. But on more accurately analysing the recorded cases, most of them are found to refer to atrophy or so-called fatty change, two conditions, that is, which are some of the most commonly occurring features of chronic wasting diseases, and are in no degree characteristic of diabetes. True, other diseases of the pancreas have also been observed in this affection, in particular independent or primary lesions, such as carcinoma of the head of the organ, and cystic dilatation of the ducts with secondary atrophy of the gland, due to occlusion of the canal of Wirsung by a stone, &c. Still these observations are much too isolated to have any significance except as pointing to accidental complications of the disease; and in at least the greater proportion of all cases the most careful and scrupulous examination of the pancreas has failed to detect any changes whatever.

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[*] Vid. Senator, loc. cit., p. 412.

[†] Andral, 'Compt. rend.,' 1856, xxx, p. 468; Conturier, 'Thèse de Paris,' No. 209, 1875; Cohnheim und Litten, 'Virch. A.,' lxvii, p. 160.

[‡] Vid. Senator, loc. cit, p. 412.

Under these circumstances an elucidation of the question may be looked for with more confidence from the results of chemical methods of investigation; and, in fact, these afford us some valuable hints. With reference to the ability of the diabetic organism to appropriate the sugar to its ends, a large number of exact experiments have been carried out, more especially by Külz,* on patients affected with the mild and severe forms of the disease. It turned out that an absolute inability perhaps never exists. Even in the severe form the excretion of sugar is not increased so as accurately to correspond with the sugar and amylaceous matters consumed with the food; in the mild form very considerable quantities can be retained and utilized. Many varieties of sugar, *e. g.* mannite, levulose, inosit, have no influence whatever on sugar-excretion; that is to say, they can be decomposed by the diabetic organism, obviously because they cause no increase of the grape-sugar circulating in the blood. True, these experiences also are inadequate for the decision of the real cardinal question, since they might equally well be explained by a diminution of the decomposition of sugar, or by an excessive production giving rise to an augmentation of the sugar-contents of the blood. As for the supposed excessive production, its occurrence would involve, according to the view previously propounded by us, *an abnormally abundant disintegration of albumen.* That the latter actually takes place in the body of the diabetic patient is proved indisputably by the *increased excretion of urea.* Only quite exceptionally is this increase absent in diabetes; it is not uncommonly so considerable that the amount of urea excreted in twenty-four hours is double or treble the normal, or even more; 100, 120, or 150 grams have repeatedly been found in the urine of a diabetic person. The source of this enormous quantity of urea is easily understood when one sees what an immense amount of flesh and other albuminous foods are usually indulged in by such persons. As is well known, the appetite increases very early, keeping pace with or following hard upon the increased thirst. The craving for food is not uncommonly insatiable, and cannot be lastingly stilled by the frequent and over-abundant meals. The voraciousness and polyphagia are simply indicative of the reaction, the answer, of the organism to the abnormal, or at least abnormally profuse, decomposition taking place within it; the enormous supply of albumen is required by the organism to repair the immense losses occasioned by the greatly augmented disintegration of albumen. By means of this supply, the body can usually succeed for a considerable time in maintaining its albuminous constituents undiminished; yet we learn from the emaciation to which most patients sooner or later, and sometimes very rapidly, fall a prey, that the albumen of the body itself is called upon to contribute to the excretion; in other words, the patients excrete still more urea than would correspond to the nitrogenous contents of the food consumed.

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* Külz, loc. cit., i, p. 38, *et seq.*

By demonstrating the occurrence of an increased disintegration of albumen, we have removed all difficulty as to the source of the excess of sugar in the blood; for quantitatively the albumen represented by the urea would, even in the most severe cases, be quite sufficient to supply all the sugar excreted on a purely meat diet. But for all that, the increased disintegration of albumen is not enough to explain the diabetes, for the very definite reason that a healthy person excretes no sugar on the same diet which is attended in the diabetic by glycosuria. Hence, although it has not yet been possible to directly prove the occurrence of a *diminution in the decomposition of sugar*, one feels obliged to make such an assumption. Only by a conjunction of the two factors, the augmented disintegration of albumen with the production of glycogen, on the one hand, and the reduced consumption of sugar, on the other, does the origin of the hyperglykæmia, and thereby of the diabetes, become intelligible.

But on further inquiring on what particular alterations these derangements of the metabolism depend, we are compelled to have recourse to mere hypothesis. As to the production of sugar, I have stated repeatedly that in all probability glycogen is first produced and then becomes converted into sugar, most likely by the aid of an amylolytic ferment. Yet we do not know, for example, what relations exist between the splitting up of albumen into glycogen and the production of fat; and still less are we acquainted with the locality, organ, or tissue in which the former change takes place in diabetes. Because the liver is the organ in which the glycogen most readily and abundantly accumulates, it was long supposed to be the principal seat of glycogen-production; but we now know that the muscles may under certain circumstances dispute with it the title of principal storehouse of glycogen, and above all we have learned to distinguish between the accumulation and production of this substance. If, however, its production is really a widely distributed function of animal cells, we have not the slightest *a priori* grounds for attributing to the liver the chief share in the diabetic over-production of glycogen and sugar. It is essentially the same with the consumption or decomposition of sugar; for it is probable enough that this is not limited to a single organ or tissue. Indeed, I am able to point to two localities in which it has been determined by precise experiments that sugar disappears under certain circumstances, *i. e.* in the liver and the muscles during violent physical exertion. With this the fact accurately demonstrated by Külz,* that the excretion of sugar in the urine of the diabetic decreases during forced muscular activity, *e. g.* rapid marches, is in perfect accordance; while the results arrived at by v. Mering throw no less light on those cases of diabetes in which the portal vein has been found at the autopsy to be impervious. It would, however, be an error to generalise the conclusions based on these experiences; for imperviousness of the vena portæ is an extremely rare appearance in diabetes, and the increased muscular exertion has not, according to Külz, a favorable influence on the excretion of sugar in all cases of the disease. But however numerous the points requiring elucidation in this domain, it may confidently be asserted that the insufficient decomposition of sugar *does not depend on an inadequate supply of oxygen.* This view, it is true, was believed to be supported by the fact often observed since

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* Külz, i. 178, *et seq.*; Zimmer has also long believed in the existence of a muscle-diabetes. Cf. 'Deutsch. Klinik,' 1873, 'D. med. Wochenschr.,' 1879, Nos. 19, 20, 21; 'Die Muskeln eine Quelle, Muskelarbeit ein Heilmittel bei Diabetes,' Karlsbad, 1880.

Reynoso's time, that severe impediments to respiration[*] are attended by the appearance of sugar in the urine; yet though I willingly admit the existence of a causal connection here, and am further ready to confess it possible that many of the methods employed in producing artificial glycosuria, *e.g.* carbonic oxide poisoning and perhaps other similar procedures which are accompanied by considerable disturbance of the circulation, really depend on an interference with the absorption of oxygen by the blood, still these phenomena are hardly applicable to human diabetes. Diabetic patients are very commonly the possessors of very well-developed respiratory organs, and very often compete with healthy persons in the digestion and utilization of fats. Pettenkofer and Voit[†] have indeed determined that the absorption of oxygen and excretion of carbonic acid in the diabetic bear no relation to their food or to their other excretions, but this is at bottom only another expression for the fact that all the nourishment taken by such patients is not utilized for the organism; as to the cause of this insufficient appropriation the analyses afford no information. Everything considered, it appears to me much more probable that the diabetic consume less sugar, owing to the absence of a *ferment* which in a normal condition initiates the further decomposition of dextrose.[‡]

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[*] Reynoso, 'Annales des sciences naturelles,' 1855, p. 120. Senator, 'Virch. A.,' xlii, p. 1.

[†] Pettenkofer und Voit, 'Zeitschr. f. Biol.,' iii, p. 380; Voit, in Hermann's 'Physiology,' vi, p. 225.

[‡] On the subject of glycogen and diabetes consult, in addition, Claude Bernard's numerous researches, some in the 'Compt. rend.,' some in his 'Leçons de physiol. expérimentale appliquée à la médecine;' also 'Sur les propriétés des liquides' and 'Sur la physiol. et pathol. du système nerveux, summed up in 'Leçons sur le Diabète et la Glykogenèse animale,' Paris, 1877; German by Posner, 1878. M. Schiff, 'Untersuchungen über d. Zuckerbildung in d. Leber u. d. Einfluss d. Nervensystems auf d. Erzeugung d. Diabetes,' Würzburg, 1859; J. Seegen, 'Der Diabetes mellitus auf Grundlage zahlreicher Beobachtungen,' Berlin, 2 Aufl., 1875; Senator, in Ziemssen's 'Handbuch,' xiii, i, 2 Auf., 1878, in which numerous references are contained.

CHAPTER IV.

THE PANCREAS AND INTESTINES.

Rarity of disease of the pancreas.—Reduction of pancreatic secretion.—Occlusion of the canal of Wirsung.—Trifling effect on intestinal digestion.—Steatorrhœa.—Experiments on animals.—Conclusions therefrom.—What becomes of the pancreatic juice when its escape is prevented.

Physiology of the succus entericus.—Pathological increase of the intestinal secretion.—Moreau's experiment.—Cholera.—The rice-water stools.—Post-mortem appearances in those dying during the attack.—The epithelium of the intestine.—Formed and chemical constituents of the dejections in cholera.—The rice-water not a transudation, but a secretion of the intestinal mucous membrane.—Explanation of the processes occurring in cholera.

The peristaltic movements of the intestine.—Their morbid intensification.—Its causes.—Purgatives.—Infective diarrhœas.—Enteritis.—Ulcers of the intestine.—Diarrhœa.—Impeded absorption of water from the intestine.—The fæces in diarrhœa.—Significance of diarrhœa for the organism.—Tonic intestinal contractions.—Reduction of the peristaltic energy of the intestine.—Its causes.—Constipation.—The gases of the intestine.—Meteorism.—Narrowing of the intestinal tube.—Results of the stagnation of the contents of the intestine.—Vomiting of fæces.—Rupture of the overdistended intestine.—Other solutions of its continuity.—Abnormal communications with other cavities.—External intestinal fistulæ.

Phthisis mesenterica.—Impediments to defæcation.—Tenesmus.—Incontinentia alvi.

In addition to the bile, another secretion, which is incomparably of more service in digestion, is poured out into the intestine at the same spot and at about the same time. This is the *pancreatic juice;* and it might be expected, in view of the great importance of the secretion, that the pathology of the pancreas would at least occupy as large a share of our attention as did that of bile-formation and excretion. This idea, however, is far from being realised; in the first place, because the liver and the pancreas present the sharpest contrast as regards liability to disease. This contrast is most striking in all *metastatic* processes. Not that the pancreas enjoys an immunity from such affections. A few tubercles may now and then be found in it in general miliary tuberculosis; careful examination may reveal a colony of bacteria or a small abscess in pyæmia or a similar infective process; and I am very far from disputing that a cancerous metastasis may sometimes find its way to this organ. But in the pancreas all these are exceptional, while in the liver they are the rule. When, for example, in carcinoma of the stomach, the post-mortem records frequently contain statements that secondary nodules have been present in the pancreas, this is usually owing to the confounding of cancerous epigastric lymphatic glands with the pancreas. This organ is very rarely the seat even of independent inflammations; parasites almost never establish themselves in it; its vessels are not in most cases attacked by amyloid degeneration; and as for the *fatty change*, so often said to occur in the gland-cells, it is very questionable whether observers have always had before them fat-granules, and not that *exquisitely granular condition* of the gland which is present in fasting, and still more markedly in starving, animals—that condition which Heidenhain* has shown to indicate an abundance of zymogen in the organ.

Still there remain a variety of conditions with which pathology must deal. In the first place, it is obvious that the pancreas will be involved in the more wide-spread *derangements of the circulation*—in general anæmia, in non-compensated cardiac lesions, and in the passive hyperæmias implicating the portal system alone. Further, extreme *atrophy* of the gland is not uncommon, and may be either active, as in the aged and in persons who have passed through prolonged wasting diseases, or passive, as the result of occlusion of the canal of Wirsung, with secondary dilatation and cystic degeneration of the lobules of the gland. In the next place, we find tumours, especially carcinomata, in the pancreas; primary tumours being decidedly commoner than secondary. A carcinoma usually originates in the head of the organ, but may extend widely through the gland-substance and displace it. Lastly, we have to take into account those factors which, though not directly affecting the pancreas, *impede*, or render impossible, *the evacuation of its secretion into the intestine.* Here must be mentioned *concretions*, ascarides which sometimes enter the ductus pancreaticus, tumours pressing on the duct from without, carcinoma of the duodenum directly occluding the orifice of the duct: but chiefly I desire to remind you of a circumstance already dwelt upon in connection with icterus catarrhalis, that every *gastro-duodenal catarrh* of sufficient intensity to occlude the ductus choledochus must necessarily render the ductus Wirsungianus impassable, since the pressure under which the pancreatic juice is secreted is not greater than that of the biliary secretion.[†] This catarrhal obstruction it is that perhaps claims the greatest pathological interest, not merely because of its great frequency, but especially because the second or accessory, smaller duct of the gland, which enters the intestine independently and is so commonly present in man, will be occluded in catarrh, while other obstacles not rarely leave it pervious.

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* Heidenhain, 'Pflüg. A.,' x, p. 557.

Let us now see what influence these different pathological processes exert on the secretion of the pancreatic juice, and consider the effects which possible quantitative or qualitative changes in the secretion may produce on digestion and the organism in general. It must at the outset be confessed that we are ignorant of the behaviour of the pancreas in cardiac lesions and in other varieties of circulatory disturbance. It is probable that in pyrexial diseases and in extreme anæmia the production of the pancreatic juice suffers equally with that of the other digestive fluids, if for no other reason, because fever patients more particularly are accustomed to take little nourishment; and, as you are aware, the pan-

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[*] Heidenhain, 'Pflüg. A.,' xiv, p. 457.

creatic secretion is not more dependent on anything than on the energy of gastric digestion and of nutrition generally. How the function of the pancreas is affected by cirrhosis of the liver, or by non-compensated cardiac lesions, we cannot even guess. Again, though statements as to the composition of the bile in the various diseases abound in the literature, there is a proportionate paucity of data with regard to the constitution of the pancreatic juice; and our knowledge, such as it is, of the changes occurring in the composition of the latter fluid is altogether due to observations on pancreatic fistulæ established by physiologists. Such being the state of the case, only one condition remains to be discussed by the pathologist—*the diminished secretion of the pancreatic juice.* That a gland which has undergone marked atrophy or been converted into a cystic tissue or been replaced by masses of cancer, cannot produce the normal amount of secretion, requires no demonstration; in the most extreme degrees of atrophy or of degeneration all secretion will no doubt cease. But this involves the discharge of too little, or of no, pancreatic juice into the intestine, and intestinal digestion must necessarily take place *without the co-operation of this most important secretion.* The same result will follow when the juice, though produced by the gland, is not poured out, owing to occlusion of the canal of Wirsung. How does intestinal digestion take place in such circumstances?

You will certainly expect that the absence of pancreatic juice should much more seriously disturb the digestive processes than would the absence of bile. The pancreatic juice contains most energetic ferments, which are capable of acting on all three chief categories of our foods, the albumens and carbohydrates as well as the fats; and there can be no doubt that, in a normal condition, it is mainly the office of the pancreas to transform all the albumen not peptonised in the stomach into substances easy of absorption, and that the organ also acts on the great bulk of the amylaceous constituents, only small quantities of which can be converted into sugar by the action of the saliva. What an energetic part is played in the digestion of fat by the pancreatic secretion has lately been dwelt on. Indeed, one might almost feel inclined to ask—Can a true and regular intestinal digestion take place in the absence of this secretion? It does take place, however, and in an astonishingly perfect manner. Human pathology, it is true, is not often in a position to afford certain information on this point, since the lesion of the pancreas is almost always associated with others which more or less severely disturb digestion. When an old person, in whom the organ is atrophied, or a patient suffering from cancer of the pancreas or duodenum, becomes emaciated, it is scarcely justifiable to ascribe this result to the absence of pancreatic juice; and in gastro-intestinal catarrh the bile is absent in addition. In the decision of this question, therefore, those cases almost alone can be utilized, where the canal of Wirsung is occluded by a stone or the like; and even then, only those instances in which the patient is free from other digestive or wasting diseases. I recently stated that stress has been laid on the occasional presence of such a condition in the bodies of diabetic persons, and at the same time remarked that in my opinion no necessity, or rather no justification, exists for ascribing to their concurrence a causal connection. On the other hand, there need be no hesitation in regarding a deficiency of the pancreatic juice as the cause of *the imperfect digestion and absorption of fats*, which has several times been observed,* and is evidenced by an abundance of fat in the fæces or even by actual *steatorrhœa*. This, however, is the only anomaly of digestion which is certainly proved to result; and even it, though repeatedly noticed, is far from constant in such circumstances. In most instances, the imperviousness of the duct or the degeneration of the pancreas, whatever its cause, is merely discovered by accident at the autopsy, there having been nothing that pointed *intra vitam* to a serious derangement of digestion;† and we meet in the literature‡ with express statements that, in spite of extreme atrophy of the pancreas, the chyle-vessels were found distended by white chyle.

These observations are supplemented in a very welcome way by experiments on animals. There is no difficulty in tying the pancreatic duct in the cat or dog, and in the rabbit the application of the ligature is one of the simplest operations. If gently done, especially under antiseptic precautions, the animals stand the operation excellently, and their condition can hardly be said to be a diseased one; the most that happens is a slight falling off in the appetite for the first few days. This is subsequently recovered, however, and when the ordinary food is then given, the behaviour of the animals as regards digestion and nutrition is precisely as before the operation. This holds equally good, you will observe, of carnivora and herbivora, nor is it less true when the occlusion has lasted long. If it be objected that in the dog the whole of the pancreatic juice is not excluded from the intestine by ligature of the canal of Wirsung, I answer that in rabbits there is no second, accessory excretory duct, neither does regeneration rapidly take place in them; at any rate, Pawloff,* working in Heidenhain's laboratory, saw no sign of a restoration of the duct during thirty days. Objections of the kind are, however, completely overthrown by some experiments carried out by Schiff,† who succeeded in producing complete atrophy and disappearance of the gland in dogs. This Bernard had failed to accomplish to his satisfaction by injecting oil into the principal duct, a result secured by Schiff by introducing melted paraffin, which quickly solidified at the temperature of the body. The animals so treated also exhibited no digestive disturbance, and in particular they could digest fat as well as ever, and when well fed underwent a perfectly normal increase in weight. Birds alone react differently to the exclusion of the pancreatic juice from the bowel. It was first of all determined by Bernard‡ that pigeons and ducks only survive the ligature of the canal of Wirsung for at most ten to twelve days. More recently Langendorff§ has discovered, by careful experimental investigation, that in pigeons the craving for food increases enormously a few days after the closure of the ductus pancreaticus, and that, in spite of this, the animals steadily lose weight because the food-stuffs taken, especially peas, are *discharged almost unaltered from the body*. It is chiefly the digestion of the *carbohydrates* that is greatly interfered with in these animals, so much so that the addition of sugar to their diet is capable of very considerably postponing the fatal issue. But this which is true of birds does not apply to mammals; the experimental results already referred to teach that in them opposite conditions prevail. I have, however, no fear that you may therefore conclude the pancreatic juice to be an unimportant digestive secretion in the mammalia; what cannot be disputed is the capacity of the mammalian organism to make good by other means the loss of the pancreatic juice, and thus to avert injury to digestion. This is partly effected, beyond doubt, by the aid of the other digestive juices. The conversion of starch into sugar is brought about by the agency of the succus entericus, and the digestion and absorption of the fats is then thrown essentially upon the bile. But there is no other digestive fluid which is capable of acting on the flesh and other albuminous bodies not peptonised in the stomach or on the peptones precipitated by the bile; and if, in spite of the occlusion of the pancreas, these substances are digested, this is due simply to the decompositions brought about by the *bacteria* which are always present in the intestinal canal, *i. e. by the aid of putrefaction*. By the agency of bacteria, neutral fats can also probably be split up in the intestine, so that there will even be no dearth of the fatty acids, by separating which the pancreas is ordinarily such an essential instrument in preparing the fats for absorption. More importance, at any rate, attaches to the fact, that the putrefactive decomposition of albumen in the intestine gives rise first to peptonoid bodies which are therefore readily absorbed, and further to bodies poorer in nitrogen, such as leucin and tyrosin, which in a normal condition are separated from albumens by the pancreatic juice.

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* Quoted by Klebs, 'Handb. d. pathol. Anat.,' i, p. 346.

† Cf., for example, Litten, '(Neue) Charité-Annalen,' iv and v.

‡ Hoppe-Seyler, 'Physiologische Chemie,' p. 358.

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* Pawloff, 'Pflüg. A.,' xvi, p. 123.

† Schiff, 'La Nazione,' 1872, Nos. 162—116, referred to in 'Med. Centralbl.,' 1872, p. 790.

‡ Cl. Bernard, 'Mémoire s. l. pankréas,' 1856, p. 533.

§ Langendorff, 'A. f. Physiol.,' 1879, p. 1.

The experiment of ligaturing the pancreatic duct is also calculated to afford information on another question of no less theoretical and practical interest, namely *the abode of the secretion when its escape is prevented*. For that the process of secretion goes on continuously after ligature of the duct has been directly demonstrated in Heidenhain's laboratory;[*] even after the lapse of thirty days there flowed from a cannula introduced into the duct a secretion which displayed no noteworthy difference as compared with the normal pancreatic juice of the rabbit, except that perhaps it was slightly less in quantity. This diminution, however, is not surprising; for a great part of the gland atrophies in consequence of the dilatation of the duct, the place of the gland-substance being taken by connective tissue abounding in lymph-cells, just as happens in the guinea-pig's liver after ligature of the ductus choledochus. But if the pancreas goes on secreting after closure of the duct, while the dilatation of the latter continues moderate in degree and is evidently incapable of affording room for the secretion even of a few days, it follows that *the pancreatic juice must be absorbed and carried off by the blood-vessels or lymphatics of the gland.* The case is precisely similar to that of the bile, though the occurrence of absorption cannot so readily be detected, owing to the colourlessness of the pancreatic juice, as when bile is absorbed with its characteristic and striking pigment. Now pancreatic juice is much less of an indifferent fluid than bile, and in particular it contains a ferment, the *trypsin*, which has the power of readily and rapidly dissolving all albuminous substances in a slightly alkaline solution, and which might therefore be expected to exert a most deleterious effect on the blood and its formed constituents. But nothing of this kind happens. There is positively nothing to indicate that any kind of abnormal process is taking place in the blood; the animals, as repeatedly stated, behave precisely as in health. The same absence of results was observed by Kühne[†] on injecting a solution of trypsin directly into a vein. As after these experiments he could detect the ferment in the urine, it is probable that the ferment absorbed from the pancreas is also simply excreted with the urine, in so far at least as it is not reconverted into harmless *zymogen*, perhaps by the withdrawal of oxygen. Not alone in the blood, however, does the pancreatic juice, usually so energetic, prove itself perfectly innocuous; it is equally harmless *in the abdominal cavity.* If, as often happens, the cannula accidentally slips out of a pancreatic fistula, the juice will necessarily escape into the abdominal cavity for a time, but without the slightest injury to the animal, without, indeed, any disturbance of the healing of the wound or of the regeneration of the injured duct. This is a fact which has been observed* by many physiologists, and is all the more remarkable as Kühne produced "the most horrible decomposition" by subcutaneously injecting the same solution of trypsin which he found to be indifferent when introduced into the blood. It is impossible to discover at present on what this dissimilar behaviour of the abdominal cavity and subcutaneous connective tissue towards the pancreatic juice depends.

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[*] Pawloff, 'Pflüg. A.,' xvi, p. 123.

[†] Kühne, 'Verhandl. d. naturhist. med. Vereins zu Heidelb.,' ii, Heft. 1.

With regard to the relations, more than once referred to, which have been supposed to exist *between diabetes and diseases of the pancreas*, it will be of interest to you to learn that Heidenhain* *has never discovered the least ground for such an assumption* in the animals experimented on by him. On the one hand, he was able by the *piqûre* to produce the most typical diabetes in animals whose pancreatic juice was conducted out of the body; and, on the other hand, he always failed to detect sugar in the urine of rabbits, in which the canal of Wirsung had been ligatured for a longer or shorter period.

Of the remaining digestive juices poured out into the intestine, the secretion of *Brunner's glands* is of little interest to the pathologist. For even its physiological significance in man is still unknown to us; and Grützner† has not ventured to decide whether the glands of Brunner, like those in the pylorus, behave as purely *peptic glands* in any other species than those examined by him, *i. e.* the dog and swine: still less are we acquainted with any sort of pathological process occurring in these glands. On the other hand, *the secretion of the glands of Lieberkühn, i. e.* the *succus entericus*, demands a thorough discussion. This juice has already a formal history. Its existence was inferred on theoretical grounds by the older physiologists, who attributed to it a very considerable *rôle* in the digestion of food-stuffs. Subsequently the prevalent ideas as to this secretion and its effects were brought within modest bounds by Thiry's well-known investigation;* and so strong has been the reaction against the old belief that doubt has recently been thrown even on the occurrence of any secretion by the intestinal wall, and in particular by Lieberkühn's glands, and this too by a highly reputable authority.† Yet such scepticism, in my opinion, overshoots the mark. The method employed by Frerichs‡—tying of a loop of intestine emptied by previous squeezing—did not, it is true, allow of his obtaining pure intestinal juice; but when a dog which has fasted for several days is taken, and a double ligature applied to a loop of intestine for some hours, after previously squeezing or, better, washing it out, I am at a loss to imagine how the more or less large quantity of fluid with which it becomes filled should be regarded, if not as *the secretion of the intestinal mucous membrane.* The idea that its source is an abnormal transudation from the blood-vessels of the intestine into the intestinal canal is negatived not only by the complete absence, after this operation, of any kind of circulatory disturbance in the intestinal walls, but especially by the anatomical arrangements of the part in question, as well as by the characters of the fluid itself. Conditions giving rise to an abnormally increased transudation from the vessels of the intestine are far from uncommon in pathology; but while an increase of the lymph-stream from the intestine, œdema of the intestinal wall, or ascites is often enough the consequence of hepatic cirrhosis, or of imperfectly compensated cardiac lesions, there is in these cases no effusion of fluid into the intestinal canal. Even for enteritis, it is by no means made out that the exuded fluid enters the cavity, so long at least as the epithelium of the intestine remains intact. That it might enter, it would at any rate be necessary that the inflammation should be accompanied by an actual exudation, and that this is excluded in the present instance is proved by the absence of all hyperæmia, and no less by the *poverty in albumen* of the fluid poured out. The albumen-contents amount to not more than a few milligrams per thousand, and even then a part is derived from the cells contained in the mucous flakes which are suspended in the fluid, as well as, no doubt, from the intestinal contents, some of which, despite the squeezing and washing, remain adhering to the mucous membrane. But who could suppose a fluid having such characters to be a transudation from the blood? You will not misunderstand me: I do not deny that fluid may under certain circumstances pass out of the vessels of the mucous membrane into the cavity of the intestine; in all ulcerative processes, all diphtheritic inflammations, *i. e.* in every case where the epithelium is destroyed, this may undoubtedly occur, and the very considerable albumen-contents of dysenteric stools teaches unmistakably that it does occur. It is also true that the fluid which accumulates in a few hours in a ligatured loop of intestine into which a few cubic centimetres of a concentrated solution of Epsom salts, Glauber's salts, or common salt have been injected[*] may in part have diffused over from the vessels of the mucous membrane, but this does not at all justify the assertion that every fluid poured out from the wall into the cavity of the intestine is a transudation from the blood. Add to all this the observations of a large number of writers,[†] made on Thiry's fistulæ, that a piece of intestine thus isolated produces almost no secretion in a fasting condition and during rest, but pours out no inconsiderable quantity of fluid on mechanical or electrical stimulation and during digestion. Lastly, should any doubt still remain as to the secretory capacity of the intestinal mucous membrane, it is set aside by the discovery[‡] in Kühne's laboratory, that the injection of 0·01 pilocarpine into a cutaneous vein is followed in a few minutes by an extremely strong and rapid flow from the Thiry's fistula.

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* Heidenhain, 'Pflüg. A.,' xiv, p. 457.

† Grützner, 'Pflüg. A.,' xii, p. 285.

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* Thiry, 'Wien. akadem. Sitzungsber.,' Math. Naturw. Kl., Feb. 25, 1864.

† Hoppe-Seyler, loc. cit., p. 275.

‡ Frerichs, 'Handwörterb. d. Physiol.,' iii, 1, p. 851.

However indubitable it accordingly is that an actual secretion, the succus entericus, is produced by the glands of the intestinal mucous membrane, it is no less certain that the *rôle* which falls to the intestinal juice in digestion is a very subordinate one. The sole fermentative action which has been noticed by the majority of observers in the succus entericus of the dog, and more recently in a case of complete fistula of the small intestine in man,* is the capacity of *converting starch into grape-sugar and of producing grape- from cane-sugar.* On the other hand, the intestinal juice has no action on fats, on cooked or raw flesh, or on coagulated egg-albumen—in fact, on most albuminous bodies. Raw fibrin is the only such substance which, according to several writers, can be dissolved by the succus entericus, and a comparatively long time is required for its solution. This result, however, is not unassailable. For if the solution is effected in an alkaline or neutral medium, it is necessary to completely exclude the co-operation of putrefaction, before the presence of a specific digestive juice can be fairly inferred; and a slight degree of solubility in an acid medium does not allow of our drawing any conclusion, inasmuch as minute quantities of pepsin have been detected by Brücke and Kühne in almost all the juices and tissues. When Masloff† added antiputrefactive thymol to the alkaline intestinal juice obtained from a Thiry's fistula, he failed in dissolving the fibrin.

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[*] Brieger, 'A. f. experim. Pathol.,' viii, p. 355.

[†] Kühne, 'Physiol. Chemie,' p. 136, 'Verhandl. d. naturh.-med. Vereins zu Heidelberg,' ii, Hft. 1; Leube, 'Beiträge zur Kenntniss des Dünndarmsaftes u. s. Wirkungen,' Erlangen, 1868; Schiff, 'Il Morgagni,' 1867, No. 9; Quincke, 'A. f. Anat. u. Physiol.,' 1868, p. 150; Masloff, 'Untersuch. d. physiol. Inst. zu Heidelberg,' ii, p. 290; Dobroslawin, 'Untersuchungen aus dem Grazer physiol. Institut.,' 1870, Hft. i, p. 73; Heidenhain, in Hermann's 'Handbuch,' v, p. 163

[‡] Masloff, loc. cit.

Such being the state of affairs, it will hardly be supposed that a diminution of the secretion of succus entericus can have any practical importance for intestinal digestion. Moreover, we do not know of any pathological process by which the secretory power of the intestinal mucous membrane is generally arrested or considerably reduced; the most extensive and numerous ulcerations of the mucous membrane always leave large surfaces, chiefly in the jejunum, undestroyed. More interest, it seems to me, attaches to the question—whether morbid conditions exist, under the influence of which *the secretion of intestinal juice becomes considerably greater, more profuse, than normal.* This question is, in the first place, suggested by a remarkable experiment devised by A. Moreau.‡ When the whole of the nerves passing in the mesentery to a doubly ligatured (previously emptied) loop of intestine are divided at some distance from the bowel, the loop becomes filled rapidly or slowly, but always within a few hours, with a considerable amount of alkaline, pale amber-coloured, thin fluid, which is turbid owing to the presence of numbers of yellowish white mucus-like flakes, and has a very low specific gravity, containing less than ·5 per cent. organic and about double as much inorganic constituents. Of the latter, soda-salts decidedly preponderate, there being present a comparatively large quantity of carbonate and bicarbonate of soda, so that the liquid effervesces on the addition of acids. Of the organic constituents, albumen forms nearly a third, while urea was also detected by Moreau. Consider in addition that Masloff was able by means of the liquid so obtained to convert starch into sugar, and you will admit that its agreement with intestinal juice is very complete. The similarity is not lessened by the presence of the above-mentioned flakes, forming as these do a characteristic constituent of the secretion of Thiry's fistula,* nor by the minute quantity of urea, since urea passes over into very many of the secretions. If this liquid were a transudation, it would be incredibly poor in albumen, even if we ignored the fact that such an abnormal increase of the transudation as the result of division of the nerves has never been observed elsewhere. Everything considered, it seems to me much more plausible to believe that in Moreau's experiment we have a *hyper-secretion* of succus entericus, perhaps paralytic in character.

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* Demant, 'Virch. A.,' lxxv, p. 419.

† Masloff, loc. cit.

‡ A. Moreau, 'Med. Centralbl.,' 1868, p. 209.

The entire question acquires an actual importance in pathology only through its bearing on one of the most remarkable and dangerous of diseases, namely *cholera*. The pathognomonic criterion of cholera is, as is well known, *the copious rice-water evacuations per os et anum,* to which the patients are subject in the choleraic attack proper, either after some days of diarrhœa or in the absence of this precursor. That the evacuations are the result solely of a copious discharge of rice-water fluid into the digestive canal, is the less necessary to prove, since in every epidemic a large number of persons perish who have had little or no vomiting or diarrhœa, yet in whose intestines litres of the characteristic fluid are found at the autopsy. In such persons the irritability of the nervous system has become so blunted, that the fluid accumulated in the intestines is incapable of exciting the act of vomiting or of defæcation. It is equally unnecessary to show specially that the fluid evacuations really form the central point of the entire disease; for, as already pointed out (vol. i, p. 466), it is these which gradually bring about that extreme inspissation of the blood which in the severest cases finally puts an end to the circulation and in this way destroys life. In order to understand cholera, therefore, it is indispensable that we should possess an accurate acquaintance with the mechanism and processes on which the discharge of fluid into the intestinal canal depends. Now, you need have no fear that I am about to bring before you the evidence *in extenso* for the view that the ultimate cause of cholera, this exquisitely epidemic disease, is to be sought in a specific *virus*—a virus which more than probably is an *organised, parasitic* one; although all efforts at finding it in the choleraic stools and dead body have hitherto miscarried. To us the only question of interest is the modus in which the human body reacts to the cholera virus after this has entered it: in other words it is our business to inquire—*whence comes the fluid which is poured out into the intestine during the attack*, and in what way, by means of what mechanism, is it poured out?

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* Leube, loc. cit., p. 359.

We may at once eliminate one possibility from our discussion, namely that the copious dejections are due to equally copious draughts of liquid. Not that the evacuations of cholera patients contain no ingesta! On the contrary, when the seizure is somewhat suddenly developed, the ordinary contents of the stomach and intestines are always expelled by the first few acts of vomiting and defæcation; and during the subsequent course of the attack the drinks taken are for the most part at once vomited. But to say nothing of the chemical differences, the notion is completely overthrown by the fact that the total amount of fluid evacuated as good as invariably exceeds the total liquids partaken of, the excess being always considerable and sometimes several times the amount taken. Moreover, the inspissation of the blood and the disappearance of the juices of the tissues indicate only too clearly the source of the rice-water. The inspissation does not admit, it is true, of any direct conclusion being drawn from it as to the mechanism of the fluid evacuations. When saliva is poured out by the litre in mercurial ptyalism, it is just as certainly drawn from the blood as is the transudation in mechanical hyperæmia or in inflammation: we have, if possible, to determine not *the fact* itself, but *the manner* in which the fluid enters the intestine from the blood. Naturally, it was at first hoped that the desired information might be obtained by an accurate examination of the intestine, as the locality affected by the disease. Opportunities for post-mortem examination are unfortunately numerous enough in an epidemic of cholera; and there are hardly any appearances more characteristic than those found after death form this disease—the tar-like quality of the blood; the dryness and peculiar leathery toughness of the lungs, muscles and other tissues; the soapy tenacious feel of the serous membranes, never to be forgotten by anyone who has introduced the finger into the thoracic or abdominal cavity of a person dead of cholera. Yet all these appearances—obviously nothing but the consequences of the rice-water stools—are not relevant to the question now occupying our attention; for us, as already stated, the *intestine* alone is of interest. In cholera this organ contrasts strikingly enough, it is true, with all the other organs, owing to the quantity of fluid usually contained in it; but it presents no other well-marked pathologico-anatomical characteristic. In persons dying during the seizure, the mucous membrane is found in a state of marked *rosy injection* and *hyperæmia*, with, as a rule, something of a *livid* tint; further, the follicles, both agminated and solitary, are usually swollen throughout and project above the surface of the rest of the mucous membrane. This latter appearance cannot be utilized in any way for the explanation of the disease, since it is very frequently met with in the greatest variety of conditions, and is present to a slight extent even during every digestive period. We shall seek in vain for hæmorrhages, losses of substance, or deposits, in short for any indisputable pathological sign. Nor is microscopic examination of any avail. One fact, it is true, and that a very striking one, is revealed by the microscope, namely *a deficiency of the intestinal epithelium*. This appearance will be the more certainly met with, the more fluid has remained in the intestine and the longer the autopsy has been deferred; it is absolutely certain to be found if the contents of the intestine have been removed by squeezing. Numbers of villi are completely robbed of their epithelial covering; the summits of others are stripped while their bases are clothed with undamaged epithelium; many others again have their epithelium perfectly intact. The abode of the missing epithelium is not far to seek. In the intestinal fluid there float, as a rule, quantities of epithelial shreds, both single cells and more especially connected cell-groups, some being pretty large membranous pieces of epithelium. A very delicate appearance is presented by the epithelial coverings of villi which seem to have been actually removed like the fingers of a glove. This extensive shedding of the epithelium was formerly regarded as, and is still held by many* to be, the distinguishing criterion of cholera from other acute diseases of the intestine accompanied by diarrhœa, to be, so to speak, the anatomical basis of this disease. And in fact if such a desquamation really takes place at the beginning, or during the course, of the attack, it cannot be questioned but that it must have the very highest significance for the entire processes of absorption and transudation from and into the intestine. But is the desquamation really a pathological process? In reply to this question, the circumstance that the epithelial cells are always found in the intestinal fluid completely unaltered, and the fact of the absolutely perfect preservation of the tissues of the naked villi are calculated most certainly to insure the opposition of anyone who knows that the shedding of epithelium is preceded at other times by certain changes in it, and that every mucous membrane reacts with extreme sensitiveness to an extensive deprival of its epithelium. All speculation, however, is rendered superfluous in cholera by the ease with which the intestinal contents may be examined with the greatest accuracy *intra vitam*; for if epithelium is shed during the attack we must necessarily find it to a corresponding amount in the dejections. Yet, however often and confidently its discovery in the stools has been asserted, this is not the case. As early as the epidemic of the fourth decade, Böhm* emphasised the absence of epithelium from the cholera stools as contrasted with the intestinal contents of the dead body. Still more, during the epidemic of 1866, many hundreds of rice-water stools were examined in the various cholera lazarettos of Berlin by Kühne, Bruberger,† Hirschberg, myself, and others; but although we all directed our attention especially to the presence of epithelium we only rarely succeeded in finding a few undoubted epithelial cells therein; and even with regard to these it was not possible to absolutely exclude an accidental contamination. Accordingly, there cannot, in my opinion, be a doubt *that the entire desquamation of the epithelium is nothing but a result of post-mortem maceration.*

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* Hoppe-Seyler, loc. cit., p. 359.

The morphotic elements of the rice-water stools are of a very different nature. They are not very numerous, it is true; but one is almost certain to find a few soft, whitish *flakes of mucus*, which consist chiefly of small clumps of colourless cells, surrounded by a gelatinous capsule; red corpuscles have not been observed in them. *Bacteria* of various forms are invariably present; yet our knowledge of the nature and properties of parasitic organisms in the year 1866 was much too imperfect to allow of our attaching any special importance to our observations in this direction. We are better informed, at any rate, as to the *chemical* constitution of the cholera-dejections.‡ Subsequently to the removal of whatever matters happen to be present in the digestive canal at the commencement of the attack, the dejections *per anum* are not essentially distinguished from the vomited material. The excess of water in the vomit, and the lower specific gravity (1,002 to 1,005) thus conditioned, depend simply on the presence in it of the liquid matters drunk during the attack. The specific gravity of the rice-water stools is, as has been said, slightly higher (1,006 to 1,013). The reaction of both is neutral or alkaline. Amongst the solid constituents, the inorganic exceed the organic, chloride of sodium being greatly in excess of other inorganic bodies, while only minimal quantities of potash salts and phosphates are present. Of organic substances, *urea* or ammonium carbonate, and *albumen* can be detected, the latter, it is true, in such minute quantities that on testing the vomit by boiling and by sulphuric acid, scarcely more than an opalescent cloudiness is produced; in the dejections the same treatment causes the separation of a few delicate flakes. But perhaps the most interesting substance contained in the cholera-dejections is the *sugar-forming ferment* found in them by Kühne;* while he was unable to detect any other digestive ferment, he never failed in converting starch into sugar by means of the rice-water stools.

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* Böhm, 'Die kranke Darmschleimhaut in der Cholera,' 1838, p. 22.

† M. Bruberger, 'Virch. A.,' xxxviii, p. 296.

‡ C. Schmidt, 'Charakteristik d. epidem. Cholera gegenüber verwandten Transsudationsanomalien,' 1850; Bruberger, loc. cit.

And now, could a fluid having this constitution be poured out directly from the blood-vessels of the intestinal mucous membrane into the cavity of the intestine? is it possible, in other words, that it is a true transudation despite its poverty in albumen, the complete absence of red blood-corpuscles, and the presence of a ferment? It appears to me that whoever maintains this, whoever takes his stand on the assertion that in cholera such a transudation could by any possibility be derived from the vessels of an intestinal mucous membrane, which is neither mechanically congested nor inflamed, but anatomically unaltered, should at least go further and devise *ad hoc* a mode of transudation differing from all known modes. On the other side of the question, the agreement between the rice-water dejections, the succus entericus, and the fluid obtained in Moreau's experiment, to which Kühne† first directed attention, is quite astonishing. For those very properties which would be so strange in a transudation from the blood, impress on the cholera-fluid the stamp of a *digestive secretion, in specie* of the *intestinal juice,* to which both as regards chemical composition and morphotic elements—the oft-mentioned flakes of mucus—it exhibits the most pronounced likeness. But if the liquid poured out during the attack into the intestine is a secretion of the glands of the intestinal mucous membrane, the rosy injection of this membrane is explained in the most plausible way; it is simply the expression of the active congestion which accompanies energetic secretion by a gland.

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* Leube, 'Beiträge,' &c., p. 11.

† Kühne, in a lecture delivered before the 'Berl. med. Gesellsch.' on March 4th, 1868, which, unfortunately, has not been published in full. 'Berl. klin. Wochenschr.,' 1868, p. 170.

From the standpoint thus arrived at, the process of cholera may be interpreted by supposing that first, under the influence of the virus, which has probably entered the intestine from without, there takes place, either with or without antecedent diarrhœa, *an extraordinarily profuse secretion from the glands of the small intestine.* The resulting rapid overfilling of the gut with fluid determines *vomiting* and *peristaltic intestinal movements.* In consequence of the vomiting, the contents of the stomach are evacuated, and afterwards the intestinal juice which has overflowed into the stomach, probably owing to its great bulk. By the peristaltic movements, the contents of the large and small intestines, and subsequently the rice-water, are expelled. Both last as long as fluid continues to be secreted by the glands and the irritability and functional capacity of the muscles in question are maintained. In favorable cases, it is probably always the cessation of the excessive gland-secretion that puts a stop to the dejections; in unfavorable ones, either the vomiting and diarrhœa persist till death, or the exhaustion of the vomiting centre precedes the paralysis of the peristaltic movements of the intestine. At any rate, the relaxed condition, amounting in some cases to *paralysis,* in which in many instances the small intestine is found post mortem does not allow of our concluding that the secretion of the rice-water was purely "paralytic," more especially as the comparatively frequent occurrence in cholera of post-mortem invaginations of the gut affords telling evidence of the persistence even after death of energetic peristaltic movements. As the result of this enormous hypersecretion, the blood becomes inspissated and the entire series of symptoms characteristic of cholera is brought about—the small thread-like pulse, the icy skin, the anuria and asphyxia, the sinking of the eyes; but the explanation of these details may safely be left to special pathology, in so far as they are not spoken of in other sections of this work. We may rest satisfied with the conclusion already arrived at; for if the view of the choleraic process just expounded be correct, it will be evident to you that a hypersecretion of intestinal juice is much more important, and attended by severer consequences to the organism than even the complete cessation of the secretion. It is, however, a no less noteworthy fact, as bearing on the physiology of the circulation, that not only are abnormally profuse losses of lymph or transudation capable of essentially altering the composition of the blood in a short space of time, but similar losses of glandular secretion can produce equally rapidly the same effect.

But supposing all the digestive juices to be poured out into the intestine, and to be normal in quantity and constitution, this would be nothing more than an indispensable preliminary to intestinal digestion. For digestion actually to take place, it is necessary, just as in the stomach, that the chyme should be *intimately mixed with the digestive juices*, and thus rendered accessible to their chemical actions. The agency by which this object is effected is well known to you; it is the peristaltic movements of the intestines. By these movements the food pulp is repeatedly mixed with the bile, the pancreatic juice, and the succus entericus; they also supply the force which ultimately brings about the emulsification of the fat by the bile and the pancreatic juice. This, however, is not the whole extent of their action. The peristaltic movements at the same time propel the chyme in the direction of the anus by a regular succession of contractions of the circular and longitudinal muscular coats. During its onward journey the chyme comes into contact with all the absorbents, one after another, of the small intestine; *i. e.* it passes over the surfaces of the villi, and whatever matters are capable of absorption are in great part there absorbed. In this again the contractions of the intestinal musculature are of considerable importance, as aiding at least in absorption by producing a positive pressure in the intestinal canal. Thus there gradually takes place a separation of the matters capable of digestion and absorption from the indigestible remainder, the former being carried into the juices of the body and the latter into the large intestine and thence into the rectum. In this way the small intestine by ridding itself of its contents, provides space for a fresh supply of food. In a normal condition, digestion in the small intestine is completed on the average in from two and a half to three hours, and consequently occupies a period which, on the one hand, is long enough to permit the action of the digestive juices on the chyme as well as its gradual absorption, and which, on the other, allows the small intestine to be emptied sufficiently soon. On the passage of the masses into the large intestine digestion proper, it is well known, is practically complete; what still takes place is mainly the absorption of any soluble salts, sugar, and peptones that may hitherto have escaped, and the gradual concentration of the chyme which has now become fæces. For this no vigorous peristaltic movements are required, and so it happens that the shorter tract presented by the large intestine is travelled through in a much longer period than was the small intestine: defæcation takes place in healthy individuals usually only once or at most twice in twenty-four hours.

As regards the conditions on which the peristaltic movements of the intestine depend, our knowledge, unfortunately, is still palpably defective.* True, it may be looked upon as certain that these movements are usually initiated in a reflex manner, the stimulation of the sensory nerves of the intestinal mucous membrane by contact with the food being transmitted to the motor nerves of the intestinal musculature. There is good reason for supposing that the centre effecting the transmission is situated in the wall of the gut itself, very probably in the Meissner-Auerbach ganglia-plexus. The sequence is usually such that stimulation of the nerves of a definite portion of mucous membrane is answered directly by muscular contraction of the same region; still it is a general characteristic of smooth muscle that the contractions extend wave-like to the neighbouring zones, so that a peristaltic contraction originating anywhere is propagated to a great distance. Further, it must be specially noted that *any* part of the gastro-intestinal canal, if strongly irritated, may be the starting-point of an extensive, or even general, peristaltic contraction. The ordinary waves in the small intestine do not, it is true, usually pass beyond the ileo-cæcal valve.* Several nerves pass to the intestine, however, and amongst them a few motor ones, yet despite the careful and minute investigations which have aimed at discovering the influence of the nerves on the peristaltic movements, it has not yet been possible to introduce law and order into this domain, more especially we have failed to discover constancy as regards excitor and inhibitory effects. Nor is our knowledge of the influence of the circulation on peristaltic action more complete. That the movements of the intestine react to changes in the blood-stream as well as to alterations of the gaseous contents of the blood is beyond dispute,† and the reaction will be more certain the more rapidly the changes take place; yet on this point too the different observations have been heretofore inconstant. But if physiology is not yet in a position to analyse the influences, very numerous as they no doubt are, to whose co-operation we must ascribe the fact that the peristaltic movements of the small intestine are so energetic while those of the large are so sluggish, you certainly cannot be surprised that we pathologists are unable to explain so many deviations from the normal course of the movements of the intestine. We do not know the nervous paths which in many individuals are subservient in causing an immediate energetic peristaltic action after certain emotional states, *e.g.* fright or anxiety, or where the transmission occurs when the same effect is directly produced by a sudden chilling or wetting of the skin. By what connection of events, putrid *intoxication*, *i. e.* the introduction of a putrid fluid into the circulation, is a violent exciter of peristaltic movements (vol. ii, p. 582) is at present quite unknown, and we are just as little able to give a proper account of the very varying behaviour of the intestinal movements in non-compensated cardiac lesions and in other diseases accompanied by mechanical hyperæmia of the portal system. We are, however, acquainted with a number of pathological factors which are capable of very considerably influencing the energy of the peristaltic contractions in one direction or the other, and their minute consideration will all the more repay us, as they are some of the most common and frequent disturbances to which these contractions are liable.

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* Cf. amongst newer researches on the intestinal movements: O. Nasse, 'Beiträge z. Physiol. d. Darmbewegungen,' 1866; S. Mayer, in Hermann's 'Handb.,' v, 2, p. 447; S. Mayer u. Basch, 'Pflüg. A.,' ii, p. 391, 'Wien. akad. Sitzungsbericht,' Math. naturw. Kl., 2, Abthl. lxii, Decb., 1870; v. Braam-Houckgeest, 'Pflug. A.,' vi, p. 266, viii, p. 163.

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* Cf. G. van Brakel, 'Pflüg. A.' iv, p. 33.

† Cf. Salvioli, 'A. f. Physiol.,' 1880, Suppl., p. 95.

If the regular peristaltic movements are the result of the stimulation of the nerves of the mucous membrane by contact with the normal chyme, it is obvious that *an augmentation of these movements must set in, either when the contents of the gut possess abnormally strong stimulating properties, or the sensory nerves of the intestine are abnormally excitable.* Amongst the unusually strong stimuli, very different agents are included. Thus a *temperature* of the ingesta differing considerably from that of the body appears to suffice; at any rate a cold enema acts more rapidly than a warm one, and in many individuals, as is well known, a glass of cold water taken fasting in the morning is enough to excite, from the stomach, energetic peristaltic action. Then the *volume* of the ingesta also plays a part, if for no other reason, because a larger number of nerve-terminations are touched at the same time: the large intestine therefore reacts much more energetically to a bulky clyster, and if a very great abundance of fluid is at once poured out, as in cholera, into the bowel, the result is an immediate occurrence of most energetic peristaltic movements. But the chief importance in these respects attaches to the *chemical* properties of the ingesta. Even among our ordinary foods are some which have had for ages the repute of acting as aperients, such as fruit, for example: and I already mentioned (vol. iii p. 904) that the bile is a decided stimulant of the peristaltic movements. This is true in a much higher degree of *purgatives.* For though numerous and varied effects have been attributed to purgatives in former and more modern times, none of these have stood the test of more accurate—especially experimental—examination, except their capacity to *excite energetic peristaltic movements.* After Thiry[*] had demonstrated on his fistula that neither laxatives and drastics, such as croton oil and senna, nor the neutral salts give rise even to the slightest discharge of fluid from the mucous membrane, Radziejewski[†] afforded, in an excellent research, the final proofs that all our purgatives, however different in nature, agree in that they vigorously stimulate the movements of the intestine, and that the varying intensity of their action depends solely on the amount of this stimulation. At most for the neutral salts it may be admitted as possible, not that they attract fluid from the blood-vessels, but that owing to their high osmotic equivalent they retain water in the intestine;* but for these salts too it was shown by Radziejewski that they certainly augment the peristaltic movements. Ordinarily—more particularly when milder laxatives are employed—stimulation of the peristaltic movements occurs only on contact with the intestinal mucous membrane itself. But the most energetic purgatives, the so-called drastics, most certainly act from the stomach, and it has long been known that laxatives when injected into the vascular system very certainly and promptly display their activity. From a pathological point of view, much greater importance attaches to the augmentation of the peristaltic movements which attends the accidental presence of substances of the most different kinds in the digestive canal. I have in mind not merely direct *poisons*, but, still more, tainted food; besides these, substances may be produced in consequence of decompositions taking place in the digestive canal itself, which violently excite the movements of the intestine. For example, after eating an abundance of sugar quantities of lactic acid may form in the intestine, or urea, excreted into it, may be there converted into ammonium carbonate. Here too belong *infective* agents. For, though a great part of the diarrhœas prevailing at certain seasons, and especially the almost epidemic variety occurring in midsummer, must be attributed to tainted food, and in children especially to milk, it seems to me no less certain that diarrhœas occur, and by no means rarely, which are exquisitely infective in character. This is in fact sufficiently proved by the fact that, in typhoid and in epidemic dysentery, diarrhœa sets in before actual ulceration takes place. I may, moreover, remind you of the diarrhœas which so often precede the actual attack of cholera, and which, during an epidemic, affect such numbers of persons who escape the cholera itself. Whether we have here simply to deal with a quantitatively slighter degree of the same infection, or with an infection by a special virus, which had been communicated at the same time with the cholera is immaterial to the question at issue, nor does it matter, so far as the infective character of these diarrhœas is concerned, whether the virus excites the peristaltic movements from the lumen of the intestine or from the blood. Finally, it may be well to mention that larger, very palpable parasites, such as intestinal trichinæ, round- and tape-worms, are capable of more or less vigorously exciting peristaltic movements, probably purely by their mechanical action.

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[*] Thiry, 'Wien. akadem. Sitzungsber,' Math. naturw. Kl., Feb. 25, 1864.

[†] Radziejewski, 'A. f. Anat. u. Physiol.,' 1870, p. 37.

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* Aubert, 'Zeitschr. f. rat. Med.,' N. F. ii, p. 225; Buchheim, 'A. f. physiol. Heilkd.,' xii, p. 217, xiii, p. 93.

In the second place, we stated, that without the co-operation of unusual stimuli, peristaltic movements will be abnormally vigorous, *when the sensory nerves of the mucous membrane are abnormally irritable.* This is necessarily the case in every marked *enteritis;* for the nerves are here continuously exposed to the pressure caused by the overloaded blood-vessels and by the increased and altered transudation; they are therefore placed in conditions which of themselves suffice to initiate evacuations, and which at any rate have the tendency to cause ordinary stimuli to be responded to by very intensified peristaltic movements. Since this applies to every form of enteritis, the acute as well as the chronic, the catarrhal as well as the diphtheritic, abnormal irritability of the nerves takes a very important place amongst the pathological causes of increased peristaltic movements. Still I desire here to state that enteritis, especially catarrhal enteritis, is not so frequent as vulgar opinion would lead one to suppose. By the laity and also by many physicians, every diarrhœa which is not the result of a purgative or the like, is regarded as symptomatic of intestinal catarrh, and enteritis catarrhalis is consequently stamped as one of the commonest diseases. But while I am not at all disposed to deny the existence of a true catarrhal inflammation of the gut, accompanied by a mucous or muco-purulent exudation, I cannot admit that, in children who perish with vomiting and diarrhœa, the intestine is always found in a state of true inflammation. For the infective diarrhœas more especially, there is the strongest inclination to seek an anatomical basis in an infective enteritis.

Yet the case is analogous to that of the purgatives. Many purgatives, *e.g.* croton oil and colocynth, may, in large doses, produce an intense, even a hæmorrhagic diphtheritic enteritis, with stormy peristaltic movements; but who would therefore suppose that the purgative action of the laxatives depended only on an intestinal catarrh set up by them? There does occur beyond doubt *an infective enteritis*, the striking symptom of which is diarrhœa; but only in a decided minority of infective diarrhœas is the intestine positively inflamed. Even the statement so frequently found in the text-books that the mucous membrane of the intestine in typhoid is catarrhally inflamed between the ulcers rests, according to my experience, on no better grounds than in the case of many other intestinal ulcerative processes. To explain the increased peristaltic action—and it was for this object chiefly that the hypothesis was adopted—the assumption is quite unnecessary; for the presence of the ulcers is sufficient explanation. However a loss of substance is produced in the intestine, nerves will always be deprived of their protective coverings and so directly exposed to pressure by other bodies, and no one can be surprised that, under these circumstances, contact even with the ordinary contents of the intestine and the normal digestive juices should suffice to set up more vigorous movements of the gut. And this effect will the more certainly follow, the more numerous the ulcers and the more widely they are distributed throughout all portions of the intestine; and the effect will also be influenced by the recent and more acute origin of the ulceration, when the ends of the nerves, and perhaps the muscles also, are still easily excitable. When these conditions are partly or altogether absent, as *e.g.* in chronic ulcerations of moderate dimensions which occupy solely the small intestine, it may easily happen, despite the presence of the ulcers, that the evacuations will not be essentially different from the normal, in number and character.*

So soon as the movements of the intestine have become abnormally vigorous as the result of any one of these very different causes, there follows what is known as *purging, looseness of the bowels, diarrhœa*. We speak of diarrhœa, as you know, when instead of the usual consistent fæces, a material abounding in water, and therefore more or less liquid, is evacuated. Such a richness in water can evidently only be produced, when either more water than usual reaches the intestine or less than usual is absorbed from it. A moment's reflection, however, at once shows that one of these two possibilities may be excluded; for the quantity of liquids introduced daily into the digestive canal of a healthy person, may vary extremely and yet the fæces remain solid; while the fact that immoderate water-drinking, though causing a great increase of the urinary secretion, does not give rise to diarrhœa is of itself proof sufficient that a mere increase of the supply to the intestine never renders the fæces watery, *provided absorption from the intestine goes on undisturbed.* This is the crucial point: the necessary fluid is more than adequately secured, even with the driest food, by the digestive juices poured out into the intestine; hence the motions must become liquid so soon as the absorption of water from the intestine is prevented or diminished. Among the causes of diminished absorption of water, I have already alluded to the possibility that the neutral salts retain water in the intestine. As to actual pathological alterations of the intestinal mucous membrane, the question obviously suggests itself, whether processes accompanied by a loss of epithelium interfere with water-absorption. This, however, is a point which can scarcely be decided, inasmuch as such processes are always complicated by inflammatory and ulcerative changes, which have just been stated considerably to augment the peristaltic movements. For the same reason, the significance of inflammatory disturbance of the circulation for the absorption of water cannot be accurately determined. On the other hand, it may be regarded as highly probable that the *mechanical hyperæmias*, so frequently occurring here, are, especially when more pronounced, prejudicial to the absorption of water; and the latter is certainly interfered with by *amyloid degeneration of the blood-vessels* of the intestinal mucous membrane, more particularly of the *villi*. This, at least, appears to me to be the most plausible explanation of the frequent and long-continued diarrhœas which form so constant a symptom of amyloid disease of the intestines, even when, on the one hand, the disease is limited to the vessels of the mucous membrane, and, on the other, there is an absence of other changes, such as inflammation and ulceration. Since, however, the absorption of water needs a certain time for its completion whether the mucous membrane be diseased in any way or completely intact, watery motions will with the greatest certainty be produced by any factor *which considerably reduces the period during which the contents of the intestine remain in contact with the absorbents.* Hence by far the most frequent cause of diarrhœa is *abnormally intensified peristaltic action.*

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* Cf. Nothnagel, 'Volkmann'sche Vorträge,' No. 200.

Consider, further, that the chyme leaves the small intestine as a more or less liquid pulp, having mostly an alkaline reaction, and a bright yellow to green colour according to the amount of bile present in it; and that only in the large intestine is it gradually transformed by loss of its liquid portions into formed fæces; and it follows that the decisive element in diarrhœa is *the increase of the peristaltic movements.* Unless the colon at the same time participates, the most active movements of the small intestine can scarcely render the motions watery, while this result may even be brought about by the intensification of the peristaltic action of the large intestine alone. Still it is by no means immaterial, especially as regards their composition, whether the evacuations in diarrhœa depend solely on increased action of the colon, or on the increase of the peristaltic movements of the small intestine as well. When the latter is the case, the motions will come to resemble the *contents of the upper part of the small intestine.* Normal human fæces* contain minute quantities of digestible, but undigested substances, such as isolated muscles-fibres, fat-cells and droplets, granules of starch; but the great bulk is composed of the indigestible constituents of the food, cellulose, elastic tissue, horny material, &c. There are present, further, the products of the decomposition of bile and cholesterin, lime- and magnesia-soaps, some rather insoluble salts; then, volatile matters—acetic, butyric, and isobutyric acids; aromatic substances—indol, phenol, and skatol, a body first isolated by Brieger.* The watery contents vary greatly with the time passed in the sigmoid flexure and rectum, but average 75 per cent.; yet fæces derived from a purely flesh diet, and especially the hard bone-fæces of dogs, may contain almost 50 per cent. of solid constituents. No undecomposed bile-pigment, glyco- and tauro-cholic acids, or unaltered digestive ferments are present in normal fæces, nor are peptone and dissolved albumen, sugar and easily soluble salts usually found therein; at most, when there is an unusually abundant supply of these substances, very inconsiderable quantities of them may pass into the fæces. All of them may be present in diarrhœa even when this depends solely on increased peristaltic action. For, in a normal condition, the absorption of these readily soluble matters continues in the colon, and it is here that the decomposition of the biliary constituents is completed. In the commencement of the large intestine it is usually easy to detect the presence of undecomposed bile, of various intestinal ferments, of leucin, alkaline chlorides, peptone and sugar. But the diarrhœic stools are much richer in these substances, even when the peristaltic movements of the small intestine are abnormally increased. Accordingly, there is no actual, sharp chemical distinction between the diarrhœas of the large and small intestine; we have to deal rather with quantitative differences. This is likewise true of the watery contents, which in the dog were observed by Radziejewski to amount to more than 90 per cent. after the administration of castor oil, senna, or Epsom salts, and which in man were determined by C. Schmidt† to be 97 per cent. after a dose of senna. In proportion to the augmentation of the peristaltic movements will be the quantity of unaltered digestive juices, and —if the digestive canal be full—of food-stuffs evacuated *per anum*; while if the stomach should share in this augmentation, many of the ingesta may very rapidly make their appearance, almost unaltered, in the motion. It need hardly be mentioned expressly that blood and pus may also be evacuated in ulceration, or in diphtheritic and hæmorrhagic inflammations of the intestine; and that in chronic catarrh* large quantities of mucus with flakes containing mucous corpuscles will be voided. I have already stated that the abundance of albumen coagulable by heat in dysenteric stools is due to their containing a quantity of inflammatory transudation derived from the vessels. It is obvious that the excrement in diarrhœa will always abound in different *bacteria*, for the development of which a very favorable medium is presented by these, usually alkaline, mixtures. Often enough, too, the well-known crystals of ammoniaco-magnesian phosphate are therein met with.

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* Very accurate morphological examinations of the fæces in various physiological and pathological conditions have recently been undertaken by Nothnagel, 'Zeitschr. f. klin. Med.,' iii, p. 241, *et seq.*

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* Brieger, 'Ber. d. deutsch. chem. Ges.,' 1887, May 28; 'Journ. f. prakt. Chemie,' N. F., xvii, p. 124.

† C. Schmidt, 'Charakteristik d. epidem. Cholera gegenüber verwandten udations-anomalien,' 1850.

Now, whatever the cause of the diarrhœa, it always involves a *loss* to the organism. In so far as the mere loss of water is concerned, this is of no importance in ordinary forms of diarrhœa, provided the body is in other respects healthy; in some affections, indeed, it may even be very desirable, *e. g.* in renal disease, where it rids the blood of superfluous water, and in inflammatory exudations where it promotes absorption by artificially condensing the blood. In the majority of diarrhœic stools, however, not only is there a loss of water, but digestive secretions and digestible constituents of the food are evacuated—substances, that is, of much higher value to the organism, which normally undergo absorption and are conveyed into the juices of the body. This consideration supplies a ready explanation of the fact that long-continued diarrhœa, far from being an inconsiderable evil, is thoroughly calculated to very considerably reduce the body. In those cases more particularly which are characterised by a marked increase of the peristaltic movements of the small intestine, intestinal digestion must almost completely succumb.

When speaking of an augmentation of the muscular contractions of the intestine, we have till now always had in mind, even when not expressly stated, those of a peristaltic character, *i. e.* which consist in a regular alternating series of contractions of the longitudinal and circular muscular coats, of such a kind that, in each portion of the intestine, the phases of shortening, narrowing, and relaxation are initiated each by one of the others. In a normal condition, in fact, this is the only kind of contraction that occurs, and artificial nervous irritation as well as disturbances of contraction, if responded to at all by the intestine, are answered by peristaltic movements. In pathology, however, we have often an opportunity of observing another form of intestinal contraction, which, as distinguished from the peristaltic form, may best be termed *tonic*. In these cases the intestinal tube is persistently *narrow and firmly contracted*, so that the lumen is almost completely obliterated or reduced to a minimum; the circumference of the tube is then considerably less than in complete inanition, when in consequence of the elasticity of its muscular coat it appears contracted and narrow. Such markedly spasmodic contractions may perhaps appear temporarily in a circumscribed portion of the intestine; but more interest and importance attaches, at any rate, to the implication of all the loops, at least of the small intestine, a condition which is always indicated on inspecting the wall of the abdomen, by a very characteristic *boat- or trough-shaped retraction of the anterior abdominal wall*. This state of tonic contraction of the entire intestinal musculature occurs, firstly, in the earliest stages of *basilar meningitis* as well as in other processes in which pressure is exerted on the pons and medulla oblongata; and secondly, it is a constant symptom of chronic lead-poisoning, *in specie* of *lead colic*. In the cerebral affections just mentioned the contraction is determined most probably by the stimulation of certain motor nerves passing from the medulla oblongata to the intestine. In lead-colic, on the other hand, it has not yet been established whether, as inferred by Harnack[*] from experiments on animals, the intestinal ganglia are directly thrown into a state of excitation by the poison, or whether, as Riegel[†] attempts to show is probable, a vaso-motor narrowing of the intestinal arteries is followed by a secondary contraction of the intestine. The action of such tonic contraction may be very simply defined; it prevents the entrance of the ingesta as far as it extends, and certainly puts a stop to the forward motion of the chyme; the result is obstinate *constipation*. On the other hand, whatever substances capable of absorption are present in the intestinal tube at the moment when the spasm sets in, will, under its influence, be certainly and rapidly absorbed.

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* Detailed information on the constitution of the fæces in intestinal catarrh is given by Nothnagel, 'Zeitschr. f. klin. Med.,' iv, Hft. 1 and 2.

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[*] Harnack, 'A. f. experim. Pathol.,' ix, p. 152.

[†] Riegel, 'D. A. f. klin. Med.,' xxi, p. 175, contains numerous references to the literature.

By the latter factor, this form of constipation is sharply distinguished from the very much more common one, which, on the contrary, depends on a *diminution of the peristaltic energy* of the intestine. If you ask, under what conditions do the peristaltic movements fall below the customary standard, I reply that very different causes may be at the bottom of it. Amongst them the chief place is occupied by all factors which tend to diminish the contractile power, and thereby the functional capacity of the intestinal musculature. Here belongs simple *exhaustion*, such as occurs, for example, after very vigorous peristaltic action; this, as a rule, speedily passes off, but may occasionally persist after purgatives have been resorted to excessively. The *muscular feebleness* of the intestine is wont to be still more pronounced in permanent circulatory disturbances, especially in chronic hyperæmia of the intestinal system of veins, and very specially when in *peritonitis* the inflammatory œdema has extended to the muscular coats of the intestine. An essentially enfeebling influence must attend every extensive alteration of the musculature, *e. g.* the fatty degeneration, which, as pointed out by Wagner,* is of such frequent occurrence in drunkards. Some other factors, though not directly impairing the contractile power of the muscular coats, may still reduce the peristaltic energy. Thus, the activity of the peristaltic movements must clearly be small when the sensory nerves of the mucous membrane are less excitable than normal. This appears to be one of the effects of opium, and at any rate is always present in opium-eaters. It might also be worth considering whether many forms of so-called *habitual constipation* may not depend upon such diminished excitability of the nerves. Perhaps there is yet another modus whereby an enfeeblement of the peristaltic contractions on a nervous basis may be brought about. In many cases of insanity and of other diseases of the central nervous system, though

* E. Wagner, 'A. f. Heilk.,' ii, p. 455.

food is taken with perfect regularity, the motions are strikingly retarded, without the occurrence of tonic contraction of the intestine; may not this retardation be due to a direct *inhibitory* nervous influence on the intestinal movements, perhaps by way of the splanchnics? Lastly, the means whereby considerable alterations in temperature of the circulating blood enfeeble the peristaltic movements, is not accurately known; in animals, whose bodies are cooled much below the normal, the peristaltic movements gradually cease, and in pyrexia the intestinal contractions take place feebly, with reduced energy, unless some other complicating factors act in an opposite direction.

As was indicated at the outset, every enfeeblement of the peristaltic movements has the necessary effect of retarding the motions, or producing *constipation*. For when these movements are weakened, the passage of the intestinal contents is retarded, and the masses do not so rapidly reach the rectum, where they should regularly excite the desire for, and act of, defæcation. Here too, it is clear, that an inconsiderable reduction of the already sluggish movements of the large intestine suffices to produce constipation, so that, as a rule, an ordinary clyster will put an end to the misfortune. Normally, only the sigmoid flexure and the upper part of the rectum are filled with consistent fæcal masses, but the latter will in this case, accumulate throughout the entire colon, inasmuch as fresh chyme is constantly being discharged into it from the ileum, but only very slowly moves forwards. The constipation is much more obstinate, however, when the movements of the small intestine are also sluggish and unenergetic, and it is more especially in these circumstances that the patients complain of an extremely troublesome sensation of fulness in the abdomen, and betray objectively the overloading of the intestines by a certain amount of distension and protrusion of the abdominal wall. In these cases, the great fulness and distension of the intestines are mainly due to a second factor, which is wont regularly to follow inadequate peristaltic action, namely, the enfeeblement and *diminution of absorption* from the gut. By what contrivances the absorption of matters contained in the intestine is effected, has not, as you are aware, been cleared up as yet, in spite of all the efforts at its elucidation: still there can be no doubt that the pressure caused in the lumen of the intestine by the contractions of the muscular coat forms an important accessory in conveying the nutritive material into the blood- and chyle-vessels of the mucous membrane; and it is also certain that the same contractions are of essential assistance in forcing on the chyle from the vessels of the intestine into those of the mesentery. Should it still be necessary to give further proofs that a weakening of the peristaltic contractions must be productive of considerable disadvantages to the process of absorption, pathology is able to produce them in abundance. Even the volume and copiousness of the evacuations taking place under these circumstances clearly tells in this sense. A very excellent illustration of the fact is afforded by so-called *cholera sicca*, to which reference was recently made. Here we saw that the overloading of the intestinal tube by a rapid discharge of succus entericus was unable to initiate peristaltic movements, because the irritability of the nerves and muscles was quickly and early destroyed. Hence the absence of rice-water stools; yet the fluid is not, as would normally be the case, absorbed, but remains undiminished in the paralysed intestine till death. By far the most instructive and demonstrative fact in connection with a paretic or paralytic intestine, however, is the behaviour of the *gases* in it.

The gases ordinarily present in the intestine, either enter it from the stomach through the pylorus, or develop in the intestine itself. That which passes into it from the stomach, can only, in a normal condition, be the residue of the swallowed atmospheric air. Since, however, practically all the oxygen is absorbed by the vessels of the gastric mucous membrane, and its place taken by carbonic acid, the mixture of gases entering the intestine from the stomach will consist only of carbonic acid and nitrogen. In the small intestine itself, gases are developed from the chyme, chiefly when the diet is vegetable, containing starches and sugar. The gases in question are hydrogen and carbonic acid, so that butyric fermentation is probably concerned in their development. Accordingly, the gases normally met with in the small intestine consist of a mixture of *nitrogen*, *carbonic acid*, and *hydrogen*; only traces of oxygen are usually present. The same gases are always contained in the large intestine, yet *marsh gas* is also found here, constantly at least after a vegetable or mixed diet; on a meat diet, traces of *sulphuretted hydrogen* often appear. All the gases which develop in the intestine owe their origin, in by far the greater part, if not altogether, to various fermentative and putrefactive decompositions, which are set up by bacteria in the contents of the intestine. It need hardly be mentioned expressly, therefore, that, in insufficiency and dilatation of the stomach, a great quantity of abnormal gases may pass directly from this organ into the intestine, and that, on the other hand, the development of gases in the intestine itself will be highly favoured by the retention in it of the food-pulp for a long period. I also mentioned recently (vol. iii, p. 905) that when the anti-putrefactive bile is absent from the intestine, the development of gas is generally specially copious.

Now if, in a physiological condition, the amount of gases present in the intestine is, despite their continuous increase, only moderate and their tension slight, this is much less an effect of the peristaltic movements, which are of service only when gas is very abundantly formed for a short time, than of the *absorption of gases*. Owing to the fact that this absorption keeps pace uninterruptedly with their development, the gases are removed into tributaries of the portal vein, to be immediately excreted from the lungs. But in order that these gases, some of which are difficult of absorption, may be taken up by the blood, the aid of the intestinal contractions will, it is evident, be very specially necessary, and while absorption is greatly furthered by the tonic contraction of the gut, it decreases so soon as the peristaltic action is depressed considerably below the normal. Thereupon the amount and tension of the gases of the intestine increase, the gut becomes much distended, with the result that what is termed *meteorism* is produced, the extreme degrees of which are known as *tympanites*. The development of marked meteorism is always an undesirable event, chiefly because, owing to the great strain on the intestinal wall, the blood-vessels running in it must necessarily be compressed and narrowed, and thus a fresh obstacle to the absorption of gases be produced. Under these circumstances, the volume of the intestines increases enormously, and the abdominal cavity becomes immensely enlarged, a change, it is true, which can only take place at the expense of the yielding walls of the cavity. In vigorous and healthy individuals, the diaphragm is much less resistant than the very powerful musculature of the anterior abdominal wall; hence in such persons the diaphragm will be driven upwards more strongly and earlier than will the wall of the abdomen outwards. Should, however, the latter be abnormally distensible, as in the puerperal state, or after the removal of a large tumour or considerable collection of fluid from the cavity, the abdominal wall may then also be distended and protruded strongly outwards.

By far the highest degrees both of meteorism and constipation are observed, when *any kind of obstacle for a length of time considerably impedes*, or even renders impossible, *the forward movement of the intestinal contents.* Such an obstacle may be produced by the accumulation of large quantities of hard fæces in the large intestine, in persons who intentionally avoid a motion, owing to painful ulcers of the anal region and the like, or who cannot voluntarily empty the rectum, owing to deficient aid from the enfeebled abdominal muscles. Much more serious obstacles exist, however, of a pathological kind. Like the other canals of the human body, the lumen of the intestine may be extremely narrowed by *tumours* and by *cicatricial strictures* resulting from deep ulcerations; foreign bodies, also, which have accidentally entered the gut—I may remind you of the large gall-stones, already mentioned (vol. iii, p. 899), may become firmly impacted and thus completely block the way. From the peculiar anatomical arrangements of the intestines, moreover, certain other causes of impermeability arise, to which there is nothing analogous in other organs: I refer to *strangulated herniæ;* further, to so-called *internal strangulations,* which may be due to the passage of a loop of small intestine through an abnormal aperture in the mesentery, or to its constriction by a band crossing the peritoneal cavity, a strong cord-like adhesion, or again to the production of a sharp bend in the intestine through the adhesion of single loops to the wall of the abdomen or pelvis; lastly, I have in mind *volvulus,* which most frequently occurs, as is well known, in the sigmoid flexure, and pathological *intussusception*, that is, the invagination of one portion of the intestine into the portion following it. No matter what the cause of the obstruction, a less than normal quantity of intestinal contents will pass the affected spot; the evacuations will therefore become infrequent and small in amount, and, indeed, if the intestine is quite impassable the motions must soon cease altogether. Above the obstacle, on the other hand, the food-pulp accumulates, and there is produced, slowly or rapidly according to the amount of stenosis, such an overloading and distension of the affected loops as to greatly damage the functional power of the muscular coat; thus, as already explained, the preliminary conditions of the most extreme meteorism are set up. Yet these are not the only results of the stenosis. Under physiological conditions the passage of the chyme through the small intestine is so rapid that the albumen of the food cannot possibly be there subject to profound putrefactive changes. The small intestine is rather the proper station for the energetic action of the digestive juices and their ferments, and the bodies formed from albumen under the influence of these ferments, peptones, leucin, tyrosin, &c., are for the most part absorbed soon after their production. In the large intestine, on the contrary, where true putrefactive processes greatly predominate, there is an absence of large quantities of albumen to undergo putrefaction. The circumstances are completely altered in stenosis, especially in the small intestine. The contents of the occluded gut then behave, as Jaffé* very properly notices, like an artificial digestive mixture kept for a considerable time in a digester; *i. e.* the albuminous bodies are further decomposed and indubitable products of putrefaction arise, more especially *indol* and *phenol*, besides volatile fatty acids and carburetted hydrogen. But since absorption though diminished is not completely at an end, the bodies so formed must pass into the urine, where the phenol is excreted unaltered, the indol as *indican*. In very many cases of stagnation of the contents of the small intestine, in consequence of impermeability of the gut or of peritonitis, Jaffé† found, in fact, that the indican-contents, and Salkowsky* and Brieger† the carbolic-acid contents, of the urine were very considerably augmented, often by ten to fifteen times the normal amount and more. Jaffé and Salkowsky found the same condition of the urine in dogs, in which they had ligatured the small intestine—an operation which the animals bore surprisingly well. When the large intestine was ligatured there was no increase of indican or of phenol, nor is there any in human urine in ordinary constipation which usually depends on the large intestine alone. The explanation of this apparently paradoxical fact is undoubtedly to be sought with Jaffé in the absence from the large intestine of material for an abundant formation of indol and phenol; accordingly, in stenosis of the large intestine, large quantities of these substances can only be excreted in the urine when, owing to the obstacle, the contents of the small intestine also stagnate.

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* Jaffé, 'Virch. A.,' lxx, p. 72.

† Ibid.

There is still another event, rightly regarded as of very ominous import, which takes place much earlier and more readily in impermeability of the small intestine than in occlusion of the colon, namely, *stercoraceous vomiting, miserere.* This terrible symptom must at first sight astonish everyone, because we do not meet with materials having the appearance and odour of fæces except in the large intestine, and are naturally unwilling to admit the possibility of a reflux from such a remote region of the gut to the stomach: moreover, if the obstacle is seated in the small intestine, how can the contents of the colon by any chance reach the stomach? Still, in cases where the cause of the vomiting is an occlusion of the colon, the fæces contained in the large intestine never pass back beyond the ileo-cæcal valve, and the vomited matter always consists of *the contents of the small intestine.* True, it is not the normal chyme, but a mass which, under the influence of the putrefactive processes just described, has acquired the characters, not of course of the solid, but of the fluid, contents of the colon. The vomiting is not produced, as has been supposed, by so-called antiperistaltic movements; rather it depends on the fact that the tension of the small intestine, which gradually increases as it becomes enormously overloaded, finally overcomes the resistance of the pylorus,—this being naturally always less than that of the occlusion,—and now by the entrance of the fermenting intestinal contents into the stomach the act of vomiting is initiated. It is also possible that the distension of the small intestine of itself excites the vomiting, when the pressure of the abdominal walls would expel not merely the contents of the stomach but those of the small intestine also.

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* Salkowsky, 'Med. Centralb.,' 1876, p. 818; 'Virch. A.,' lxxiii, p. 409.

† Brieger, 'Med. Centralbl.,' 1878, p. 545; 'Zietschr. f. klin. Med.,' iii, Hft. 3.

If the interruption of the lumen of the gut be seated low down in the sigmoid flexure or rectum, the stercoraceous vomiting may, as already stated, be long delayed; in this case, however, other no less serious consequences are wont to set in the earlier. The enormous dilatation gradually undergone by the entire colon renders its wall extremely anæmic, while *diphtheria*, with attendant ulceration, is developed under the influence of the bulky and acid putrefactive products derived from the intestinal contents, which are then represented by a thin, fermenting pulp of penetrating and most repulsive odour. The ulcers having formed, it will not be long before one of the defective and thinned-out portions *ruptures*. Only a very minute aperture is usually produced; still the escape of the smallest drop of the intensely putrid fæces suffices to bring about a fatal peritonitis. A large proportion of the patients suffering from cancerous stenosis of the rectum perish in this way, and usually it is a peritonitis so originating that puts an end to the life of children who have come into the world with atresia ani, and have not been operated on.

Obviously, every other variety of *solution of continuity* of the intestinal wall must also be followed by a fatal peritonitis, provided no adhesion between the gut and some other part prevents the escape of the intestinal contents into the peritoneal cavity. Ulcers, however conditioned, are by far the commonest cause of solutions of continuity; in typhoid, tubercular, diphtheritic, and cancerous ulcers, in short in all possible forms of ulceration, we can often enough discover *perforation*. Only very exceptionally, however, at least in diphtheritic ulcers, have we to deal with actual perforation, *i.e.* with the extension of the ulcerative process to, and through, the serous coat. The final solution of continuity depends as a rule on the *rupture* of the greatly attenuated base of the ulcer, a rupture which probably is most readily occasioned by a sudden distension of the implicated loop by the development of gases or some similar cause. In the next place, *traumata*, especially when occasioned by a diffused force, *e. g.* the wheels of a vehicle, or the manipulations in forced taxis of a hernia, may produce rupture of the intestine; moreover, in volvulus and internal strangulation, gangrene of the strangulated part may allow of *linear rupture* of the affected loop. While in all these cases, there is not sufficient time for the development of digestive disturbances, such disturbances are also of decidedly subordinate importance when the perforation takes place into another cavity. Some of the varieties of this accident have been noticed already, *e. g.* the establishment of a communication between the duodenum or colon transversum and the bile-passages, the significance of which was considered in connection with the abode taken up by the bile. The cholecystitis, perhaps set up in consequence of the communication, may evidently be the more safely neglected, as this affection is wont as a rule to precede the perforation. We also noticed, further, the escape of gastric contents into the large intestine as the result of an abnormal communication between stomach and colon, and this statement may now be supplemented by saying that *the contents of the large intestine may sometimes enter the stomach* and give rise to actual stercoraceous vomiting, in the absence of all other symptoms of stenosis of the intestine. Perforation of the intestine into the pelvis of the kidney, or, as more commonly happens, into the summit of the urinary bladder, may occasion a formation of calculi, provided very severe forms of pyelitis or cystitis do not previously develop. In communication between the fundus of the urinary bladder and the rectum, cystitis is also present, but in this instance there is in addition a very troublesome symptom—inability to retain the urine. The largest contingent to these abnormal communications is supplied by the female sexual organs, not so much in consequence of the fistulæ between vagina and small intestine, sometimes produced by operative interference in difficult labours, as of cancerous disease giving rise to a large opening between the vagina and rectum. Bearing in mind the anatomical position of the vagina, these fistulæ may evidently be regarded as being equivalent to direct communications between the intestinal cavity and the exterior of the body, or external intestinal fistulæ.

Such *external intestinal fistulæ* are far from rare. They result either from traumata, by which the abdominal wall is opened at some spot allowing the intestine to protrude, or in consequence of strangulation and gangrene of a hernia with secondary rupture of the sac; moreover, they are often artificially established in incarcerated, irreducible herniæ, and above stenoses of the gut. It need hardly be said that such an anus præternaturalis is under all circumstances extremely burdensome, owing to the escape of intestinal contents, which can never be quite avoided, so much so that in true fæcal fistula of the large intestine the sufferer is almost excluded from the society of his fellow-men by reason of the bad odour; as to the amount of digestive disturbance thus conditioned, everything depends upon *whether the fistula is or is not complete*. In the latter case, *i. e.* when, though an opening leads outwards from the loop of intestine to the exterior of the body, the passage through the intestine is free and unobstructed, the fistula, according to its size, gives rise only to a small or more abundant loss of digestive juices and nutritive material—a loss, for the rest, which can be considerably reduced if not entirely stopped by properly fitting pads; still digestion takes place regularly if no other complication interferes, and nothing can be simpler under these circumstances than the compensation of the loss of nourishment by correspondingly increasing the supply. As compared with such fistulæ, much more serious and important effects attend on those by which the connection between the upper and lower segments of the intestine is completely interrupted at the affected spot, so that the ingesta travel only so far, the lower segment of the gut being then completely useless. These cases of complete intestinal fistulæ have long excited the interest of physiologists and pathologists, owing to the information supplied by them as to the process of intestinal digestion; hence the literature contains a large number of good and careful observations.

The injury resulting to digestion, and hence to the organism as a whole in consequence of complete intestinal fistula, is naturally greater the nearer the fistula lies to the pylorus, and the less therefore the length of intestine taking part in digestion. The, in a measure, classical example of a high fistula of the gut is that of Busch,[*] where the opening was situated in the upper third of the small intestine, probably not much beyond the papilla duodenalis. Within six weeks, the patient, a woman of thirty-one, had wasted to a skeleton, weighing less than seventy-five pounds, and had grown so feeble that she could not even turn in bed without assistance, and spoke with difficulty and in a whisper; respiration was quite shallow, the pulse slow and thready. Although the ward was kept warm, she had constantly a marked sensation of cold, and was in the highest degree apathetic and drowsy; it was also very interesting, that although she consumed a great quantity of food she was never completely satisfied, but remained hungry even when she felt the stomach full. None of these severe symptoms was present in Braune's case,[†] when the fistula was seated 24 centm. above the ileo-cæcal valve. This patient, a woman of forty-nine, also had become emaciated and feeble during the previous year, yet her condition did not nearly approach that of the case above described, and at any rate it was found possible to so strengthen her by a good and abundant diet in a short time, as to justify an attempt to cure the mischief by operation. Ewald's patient,[‡] whose fistula probably lay in the lower third of the small intestine, was also saved by careful nursing and a liberal dietary; nor in the cases of Markwald[§] and Czerny[‖]—complete fæcal fistula in the commencement of the large intestine and fistula of the sigmoid flexure—was there any emaciation or feebleness worth noting.

In all these examples, the lower portion of the intestine was completely inactive; motions *per anum* were altogether absent, or at most the evacuations, consisting of greyish-white lumps of mucus, were minute and took place at intervals of several weeks. The upper end, next the fistula,

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[*] Busch, 'Virch. A.,' xiv, p. 140.

[†] Braune, 'Virch. A.,' xix, p. 470.

[‡] Ewald, 'Virch. A.,' lxxv, p. 409.

[§] Markwald, 'Virch. A.,' lxiv, p. 505.

[‖] Czerny und Latschenberger, 'Virch. A.,' lix, p. 161.

of the lower segment was scarcely moist, and fluid never escaped from it. Yet this inactive portion of the intestine retained its functional power. True, such an isolated piece of the gut could not be expected to exert considerable chemical effects on the food-stuffs introduced into it. The only secretion here poured out is the succus entericus, the sole fermentative action of which is, we were able to determine, the conversion of starch into sugar. For the rest, Markwald could not convince himself, in his case, that a sugar-forming ferment is ever produced in the large intestine; the juice expressed from a sponge, which had been introduced into the fistula, failed to convert starch into sugar, and a gauze-bag filled with starch-solution gave no sugar-reaction after it had remained several hours in the large intestine. On the other hand, Busch succeeded in detecting the amylolytic ferment in the lower section of the gut in his example of intestinal fistula. No other ferment is present beyond the pancreas; and if Busch also succeeded in determining a loss of weight—sometimes only 5 to 6 per cent. and never more than 35—in pieces of flesh and hard-boiled eggs introduced through the fistula into the lower end of the intestine and left there for a considerable time, the penetrating odour of putrefaction given off by the pieces, even after six or seven hours, betrayed the agency to which the loss was due. In this respect more especially, these cases of human complete intestinal fistulæ are extremely instructive. For they show not only that true and indubitable putrefactive processes take place in the human intestinal canal, but above all that these putrefactive processes are actually beneficial to the organism, owing to the absorption of the peptones, &c., which are produced by them. The capacity for absorption of the lower section of the intestine continues as usual, in spite of the long period of inactivity. When Busch introduced gruel and meat-broth, beer, pieces of egg and meat into the lower segment, the patient after twenty-four hours had an abundant, of course clay-coloured stool, which smelt of carrion; and she recuperated remarkably in a very short time on this régime, her weight increasing in three months by nearly nineteen pounds. Not even an approximately equal effect can result from absorption from the large intestine. From it are absorbed water, peptones, sugar, and easily soluble salts, but only in small quantity and very dilute solutions, while concentrated peptone-solutions give rise to diarrhœa. Absorption here takes place very slowly; for 250 c.cm. water twelve hours were required by Markwald's patient, and Czerny calculated that the entire colon of his patient was capable at most of absorbing six grams of soluble albumen in twenty-four hours.* In another respect these results are of great value. For it is obvious that these six grams of albumen are much too small an amount for the continued maintenance of life; and although it is not impossible that other individuals may have the power of absorbing more from the large intestine, especially when suitable solutions of albumen are selected, yet these experiences render it highly improbable that we shall ever succeed in feeding for a considerable period *per anum*, if nothing whatever is taken *per os*. On the other hand, in temporary obstruction to the regular supply of food, and also in insane persons who refuse to eat,† feeding by enemata composed of the Kühne-Leube "flesh-pancreas-solution" or other solution of peptone may prove of the greatest service, and in certain circumstances be the means of saving life.

Whether, when the intestine is normal in condition, the *absorption* of food-stuffs may be checked and impeded by any kind of morbid factor unconnected with the gut, cannot at present be stated with certainty. The chyle-stream in the mesenteric chyle-vessels and in the ductus thoracicus would chiefly come up for consideration here. True, it is not open to doubt that an *impermeability of the duct* which fails to be compensated by the development of collaterals must render the further absorption of fat completely impossible, from the moment when the tension in the tributaries of the chyle-vessels has reached a certain elevation. Such impermeability, however, though not so unheard of as was formerly supposed, is yet a rare condition, and, moreover, when present is usually found associated with other severe affections, such as general tuberculosis and carcinosis, so that the condition itself has scarcely any practical interest. At any rate, it would be of much greater importance to know the degree of disturbance of absorption which may attend *non-compensated cardiac lesions*. For a disturbance of this process may be the more certainly premised here, as both the efflux of venous blood and, owing to the positive pressure in the vena cava, the chyle-stream will be impeded; as a result the vicarious office of one or other of these paths is excluded. Lastly, diseases of the mesenteric glands, especially their extremely common *caseation*, are deserving of mention in this connection. Should the caseation, as so often happens, be accompanied by tuberculous or scrofulous ulcers of the intestine, its significance can scarcely be accurately estimated. But every one who has often had opportunities for examining the bodies of little children, who have perished with the symptoms of chronic intestinal catarrh and general atrophy, knows that in them the changes in the intestinal canal fall into the shade beside the striking enlargement and caseous metamorphosis of the mesenteric lymphatic glands. In such cases, in my opinion, the idea obviously suggests itself that the true central point of the affection consists in the interference with absorption brought about by the disease of the glands, thus completely justifying the name of *phthisis mesenterica*.

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* Czerny und Latschenberger, 'Virch. A.,' lix, p. 161.

† Jessen, 'Med. Ctbl.,' 1878, p. 612.

I may be permitted, in conclusion, to say a few words with regard to defæcation, since in it some factors play a part which have hitherto not been touched upon. Close above the anus are placed, as you know, the two sphincters, by whose tonic contraction the lower end of the intestine is kept closed, and a kind of reservoir formed above in which the fæces may collect. So soon, now, as the fæces, moving downwards, touch the mucous membrane in the region of the sphincters, the tone of these muscles is reflexly increased; while, on the other hand, the desire to go to stool arises. The external sphincter is then voluntarily relaxed, and if the fæces are soft an energetic peristaltic contraction of the large intestine suffices to expel the contents of the reservoir through the anus. When the fæces are solid, the expulsive power of the abdominal muscles is called upon for aid; this vigorously presses forwards the contents of the colon and thus forces out the excrement, while the simultaneous contraction of the levator ani prevents the prolapse of the rectum itself. With these physiological factors in mind, there can be no difficulty in explaining the derangements of defæcation which are met with. If stimulation of the sensory nerves of the mucous membrane in the region of the sphincters sets up the sensation of need for defæcation, it is evident without further explanation that there will be an extremely troublesome and tormenting *tenesmus* in painful inflammation, and more especially in ulcers, of this region. It is equally unnecessary minutely to refer to the drawbacks resulting to defæcation from a relaxation and diminution of contractile power in the abdominal muscles. When the abdominal wall is greatly distended and more than normally tense, during the latter months of pregnancy or in consequence of a large ovarian tumour or a considerable ascites, and when, after the expulsion of the fœtus, the removal of the tumour, or the drawing off of the fluid, the abdominal muscles have not had time to recover their original tone—still more when they are paretic or even paralytic—defæcation in such persons depends solely on the peristaltic movements of the intestine; hence these conditions may gradually lead to such a stagnation and accumulation of solid, hard fæces in the rectum, sigmoid flexure, and descending colon as themselves to constitute, as already mentioned, a marked obstacle to the forward movement of the intestinal contents. Furthermore, it is evident that all enfeeblement of tone of the sphincters, and especially the *paralysis* of these muscles which occurs in many diseases of the spinal cord, must interfere with the retention of the fæces. Firm masses will not therefore escape, but the evacuation of softer, pultaceous excrement may be brought about solely by the peristaltic contractions of the intestine, and without the aid of the will; there occur, in other words, involuntary motions, *incontinentia alvi*. Owing to the paralysis of the sphincters, the patient, despite every effort, cannot retain the motion, and accordingly this condition should be distinguished from the other form of *sedes insciæ*, where the motion is involuntary because, owing to anæsthesia of the rectum or from general insensibility, he remains unconscious of the need for defæcation. Lastly, it follows, from the above considerations, that the relaxation of the sphincters must predispose to *prolapsus recti* in proportion as the levator ani is involved in the paresis.

SECTION IV.

THE PATHOLOGY OF RESPIRATION.

On now turning to the pathology of the respiratory apparatus, you will hardly expect me to preface this portion of our subject by an introductory exposition of the mechanism and chemistry of normal respiration, for I should only have to repeat matters with which you are already perfectly familiar from your physiological studies. It is true that if anywhere, then certainly in the domain of respiration, the relations between physiology and pathology are so intimate that not merely has the physician felt tempted to directly deduce the derangements of the respiratory apparatus observed at the bedside from the physiological doctrines of respiration, but there is the greatest difficulty in determining the boundary line between them; in fact, it is hardly possible to do so. That particular deviation from the normal which plays so important, I would say, so determining a *rôle* in all diseases of the respiratory organs—I mean the *dyspnœa*—is a process, the details and conditions of which have been most carefully analysed by physiologists. More than this; physiology concerns itself very particularly with the state of the respiration under conditions differing completely from the ordinary ones; I remind you of what you have been taught as to the respiration of artificial gas-mixtures, whether abnormally rich in oxygen or in carbonic acid, further with regard to the poisonous gases, as well as with reference to respiration under abnormally high or abnormally low atmospheric pressure. With affairs in this position we shall act most advantageously, it seems to me, if we confine our discussion to such conditions, *when due to true and indubitable morbid processes in the organism.* The path alo[illegible]h we must proceed will appear very naturally, on recollecting the individual phases of the respiratory process and the functions in which the organism thus engages. Respiration consists in an *equalisation of tension between the gases of the blood and of the atmosphere,* an equalisation which, though it may occur in any locality in which blood-capillaries come into sufficiently close contact with a stratum of air, in human beings takes place so preponderatingly in the specific respiratory organs—and here in the *alveoli*—that every other kind of respiration may in comparison be neglected. Atmospheric air reaches the alveoli through the complicated system of *respiratory passages;* and certain muscular movements, the *respiratory movements,* secure that fresh quantities of air shall constantly be brought into contact with the blood-capillaries, while at the same time the *circulation* no less constantly conveys fresh portions of venous blood into contact with the atmospheric air. If the atmosphere contains its ordinary constituents in their proper proportions, respiration will take place normally, provided the respiratory passages are natural and the respiratory movements as well as the circulation are regularly carried on. Our task will therefore be to examine the state of respiration *in abnormal conditions of the respiratory passages, in irregularities of the apparatus carrying out the respiratory movements, and in disturbances of the blood-circulation.*

CHAPTER I.

THE AIR-PASSAGES.

Anatomical arrangement of the air-passages.—Narrowing of the nasal cavity and of the pharynx.—Stenoses of the larynx and trachea.—Foreign bodies and tumours.—Goitre.—Strictures.—Croup.—Œdema glottidis.—Paralysis of the glottis-closers.—Spasm of the glottis.—Consequences of stenoses.—Death by asphyxia.—Modification of respiration.—Expiratory and inspiratory dyspnœa.—Self-regulation of respiration by the vagus.—Regulation of the amount of air respired by the dyspnœa.

Narrowing of the bronchi.—Asthma bronchiale.—Bronchitis catarrhalis and crouposa.—Mode of respiration in bronchitis.—Local bronchial stenoses.—Foreign bodies.—Tumours.—Narrowing due to cicatrices and callosities.—Obliteration of a bronchus.—Consequences of local bronchial stenoses to respiration.—Compensatory inflation of the pervious sections of the lungs.—Atelectasis and secondary bronchiectasis beyond the occluded portion of a bronchus.—Alveolar ectasis, emphysema, and bronchiectasis beyond a stenosis of a bronchus.

Obstacles in the alveoli.—Brown induration of the lungs.—General pulmonary œdema.—Inflammatory infiltration.—Hæmorrhagic infarct.—Pulmonary hæmorrhage.—Tumours.—Interstitial and cirrhotic processes.—Compression of the alveoli.—Impediments to the change of volume of the alveoli.—Pleuritic synechia.—Open, sacculated, closed, and valvular pneumothorax.—Transudations, exudations, and tumours in the thorax.—Deformities of the thorax.—Influence upon inspiration, of factors encroaching on the thoracic cavity.—Partial atelectasis.—Volumen pulmonum auctum and pulmonary emphysema.—Regulation of the *amount of air respired by changes in the mechanism of respiration.*

Importance of the air-passages as regards temperature and purity of the respired air.—Penetration of dust and larger foreign bodies, as well as of morbid products, into the lung.—Sneezing and coughing.—Localities from which the coughing-reflex may be set up, and the conditions on which it depends.— Whooping-cough.—Expectoration.—Importance of coughing.—Its consequences to the circulatory and respiratory apparatus.—Non-occurrence of coughing.

Diseases of the lung due to inhalation of dust.—Anthracosis, siderosis, and chalicosis pulmonum.—Slaty induration, peribronchitis fibrosa, cirrhosis of the lung.—Vagus-pneumonia of the rabbit.—Pneumonia in man, due to foreign bodies and leading to abscess.—Inhalation of schizomycetes.—Putrid bronchitis.—Dissection of infarcts.—Pulmonary gangrene.—Tuberculosis.—Other infective diseases.

If the atmospheric air is to arrive in suitable quantity and composition at the seat of respiration, *i. e.* the respiratory surface of the lungs, it is absolutely necessary that *the road through the air-passages should be unobstructed,* that these canals should be pervious. However varied and dissimilar is the anatomical structure of the different sections of the respiratory canal, these dissimilarities, you are aware, exert no influence on the constitution of the air as it passes ; so that for the purpose of our discussion we have to consider chiefly whether in particular portions of the respiratory tube the *entire* inspired or expired air-quantum flows through, or only part of it, *i. e. whether the respiratory tube is simple or branched.* It is, as you know, branched, on from the bifurcation of the trachea, dividing at first into a few large, and then gradually splitting up into smaller and more numerous, canals; on the other hand, as far as the termination of the trachea the air-passage is simple and undivided. The first section of the air-passage, however, may be said to occupy a kind of peculiar position. For we have, not one, but two *nasal cavities,* which are normally both of them utilized for the inspiratory and expiratory stream; and we may properly ask, What influence does the narrowing of one of the nasal cavities exert on respiration ?

Obstructions of the kind are far from uncommon; tumours, fractures of a turbinated or nasal bone, indeed a severe catarrh with abundant tenacious secretion, may greatly encroach on or completely occlude the lumen; and if under these circumstances less air were actually breathed, this would be of importance, as so much less air would be supplied to the respiratory surface. The nasal cavities are so roomy, however, that each of them can without difficulty permit the entrance of the amount required for the regular interchange of gases, and there need be no noticeable modification of breathing in order to convey to the lungs through a single nasal cavity the same quantity of air which usually enters through both. Still more, both nares may be completely obstructed and the physiological means of access to the air-passages be consequently closed without any danger to the individual. For when the supply through the nose is shut off, the mouth is opened; and we see people, with both the nares plugged on account of profuse hæmorrhage, or with both the nasal cavities blocked by a thick secretion or other cause, who constantly keep the mouth open day and night. Except an unpleasant feeling of dryness in the mouth and the well-known alteration of the voice, strangely termed "nasal," no disadvantage attends this mode of respiration; in particular, the affected individual early acquires the power of so controlling and regulating the respiratory movements that there is no difficulty when the mouth is employed in eating. Only in children at the breast does considerable difficulty arise, so that, solely on this account, a violent and especially obstinate cold in the head may for such children prove anything but a trifling affection.

The undivided section of the air-canal commences with the *pharynx*. From this point on there is no second path for the air-stream, even as a resort in case of necessity, and any factor which obstructs the passage through this section must necessarily be of considerable importance for the respiratory process. True, narrowing of the pharynx itself, sufficient to absolutely block the air-stream, is only exceptionally met with. It may sometimes happen indeed that an excessively large piece of food, if forced into the throat, becomes impacted in the pharynx, or that in paralysis of the constrictors, as already pointed out (vol. iii, p. 15), a mass suddenly carried behind the velum cannot be transported farther. There is then obviously an imminent danger of suffocation. In addition to such accidents, voluminous tumours are the only factors constituting an actual hindrance in the pharynx to respiration. They act precisely as do the very much more common and therefore more important obstructions to respiration which are situated in the *larynx* and *trachea*.

The frequent occurrence of obstruction in these portions of the respiratory canal is sufficiently explained by the comparative narrowness of its lumen, which especially at the glottis is necessarily reduced to the smallest limits. Hence the great danger attending the presence of *foreign bodies* which have by mischance become impacted in the rima, or of small *tumours*, such as are not uncommonly met with in the form of papillomatous polypi or of more compact and solid growths. These tumours are most dangerous when, originating in a vocal cord, they occupy the glottis itself and more or less fill it up; but polypi situated a little above or below the rima may also prove most pernicious, especially when provided with a pedicle sufficiently long to allow of their being forced against the glottis during inspiration or expiration. In the lower half of the larynx and in the trachea, larger tumours are necessary to produce actual stenosis: such cases are not exactly frequent, but when they do occur their import is all the more evil, as we have usually then to deal with carcinomata which have either originated primarily in the larynx or have penetrated the air-passage from the pharynx or œsophagus. Tumours of neighbouring organs may also produce narrowing of the larynx, and especially of the trachea, in another way, namely by compression from without. Among the manifold tumours of the neck, *goitre* is that which most frequently gives rise to such pressure, so much so that the so-called *scabbard-form* of the trachea has long been regarded as almost characteristic of goitrous patients. Rose,* it is true, has recently maintained that lateral compression of the windpipe is much less dangerous than *partial softening from pressure-atrophy*, to which the cartilaginous rings gradually succumb under the influence of the goitre; for as a result of this softening complete angular deviation is said to occur. This observation is in itself quite correct. If the larynx and trachea of a person who has long laboured under a large goitre, more especially if unequally developed on either side, be removed post mortem, and the attempt be made to rest it on the larynx as base, the trachea usually bends over almost at a right angle to one side at the level of the first cartilaginous ring, while a normal trachea remains straight and perpendicular. At the bend, the cartilaginous rings feel quite soft and inelastic, without our being able as yet to say exactly on what this change of consistence depends. A disappearance of the cartilages is certainly out of the question; indeed, I have found them no thinner than the rings which have retained their normal powers of resistance, so that most likely we have to deal here with a chemical change in the intercellular substance of the cartilage. Moreover, there can be no doubt that, as the result of this "flaccid softening," so called by Rose, a sudden bulging inward of the wall of the tube may occur *intra vitam*, if the head be incautiously moved, and especially if it be allowed to fall through muscular feebleness; and the deaths which have often been observed after the extirpation of a goitre, accompanied by the most obvious signs of suffocation, are naturally explainable by this fact. Nevertheless, however valuable the recognition of goitrous softening of the cartilage, it would be unjustifiable completely to ignore the importance of the long-known compression of the trachea in goitre. The sword-sheath trachea is undoubtedly more or less *narrowed* as compared with the normal, and the narrowing is greater when, as in the case of unilateral goitres, there occurs in addition a bowing of the organ to one side.

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* E. Rose, 'A. f. klin. Chirg.,' xxii, p. 1, xxvii, Hft. 3. Vid. also Maas, 'Bresl. ärztl. Ztsch.,' 1880, No. 13.

The lumen of any part of the larynx or trachea may be narrowed by *callous cicatricial strictures*, such as sometimes result from wounds or operations, occur after lupus, and most frequently of all in consequence of *syphilis*. It is obvious that such obstacles, also, will prove most dangerous if situated in the region of the rima glottidis; yet the importance of this narrow channel becomes much more strikingly apparent *in acute inflammations* of the upper air-passages. In children, the symptoms of marked stenosis of the glottis may develop even during the course of an ordinary catarrhal laryngitis, either as the result of considerable swelling of the mucous membrane or owing to the occasional accumulation of secretion about the rima. The attacks usually take place at night, and though as a rule they quickly pass off, they commonly give rise to no little anxiety on the part of the child's friends, owing to a certain resemblance to the symptoms of true croup. Very much more important than these attacks of so-called pseudo-croup is true *croupous* or *diphtheritic laryngitis*, the membranes produced in which may give rise to extreme narrowing or even complete occlusion of the rima, not merely in children but in adults. While in laryngeal croup it is the exudation that blocks the air-passage, in a second, if possible still more dangerous form of acute inflammation—so-called *œdema glottidis* or phlegmone laryngis—the same effect is produced by the great swelling caused by the inflammatory infiltration of the mucous and submucous tissues. The situation of this inflammatory œdema, or of this phlegmon, is usually the whole of the aditus laryngis; sometimes the mucous membrane of the epiglottis and of the glosso-epiglottidean or of the aryteno-epiglottidean folds is swollen into large projections, at another time the swelling involves more the arytenoid cartilages themselves and the false or true vocal cords, at a third all these parts are implicated together: but as regards the impediment to the entrance of air, no essential difference results from these slight local variations. In the lower portions of the larynx and in the trachea, actual stenosis is never occasioned by acute inflammatory processes; unless, indeed, we include here the *growth of granulations*, such as sometimes project into the windpipe from a healing tracheotomy wound, and may, it is true, attain the size and importance of small tumours.

The peculiar position of the glottis in the upper air-passage is owing, not so much to its narrow calibre, as to the circumstance *that the air-tube is here* very far from remaining constant and equal in the diameter of its lumen, but is, on the contrary, *extremely variable in width*. The shape of the rima is controlled by the action of muscles, of which, as you know, there are two kinds, *openers* and *closers*, the posterior crico-arytenoid muscles and their antagonists, the lateral crico-arytenoid, the thyro-arytenoid, and the arytenoid; all these are supplied by different twigs of the recurrent laryngeal nerve. While it is essential to phonation that the rima glottidis should be completely closed in its posterior section, and reduced to a narrow slit in its anterior vocal part, the regular process of respiration depends, on the contrary, on the glottis being open. During free normal breathing the rima, as you know, stands widely open; yet complete bilateral paralysis of the recurrent laryngeals in no way hampers respiration, because when the muscles of the vocal cords are all of them paralysed the glottis remains immovably fixed in the position assumed by it in the dead body, *i. e.* it forms a tolerably widely gaping fissure. Impediments to respiration may rather be the result either of inaction of the glottis-openers or of an abnormally strong and persistent action of the closers. The latter, the abnormal activity of the closers, is, as may easily be perceived, the really dominating element in the case; for paralysis of the openers leads to a narrowing of the rima only when their antagonists have become tonically contracted and thus permanently obtained the preponderance. Hence it may be doubted whether, as is often assumed, an acute paralysis of the glottis-openers as the result of inflammatory œdema in croup still further enhances the danger of stenosis of the rima. But if this is doubtful, we are the more certain, as the result of fairly numerous observations, as to the series of symptoms occurring in isolated *bilateral paralyses of the postici*, in which the glottis forms a narrow slit, allowing of resounding and strong phonation, yet in deep inspiration, for reasons presently to be discussed, not only does not dilate, but contracts still more. Paralysis of the postici is only exceptionally myopathic in its nature, yet in but few cases have we succeeded in discovering the cause of the paralysis of this particular branch of the recurrent nerve. We are no better situated in this respect in what, if you will, may be regarded as the directly opposite affection—stenosis of the glottis due to *spasm of the glottis-closers*. That the closure so promptly following the inhalation of chlorine, the fumes of ammonia, hydrochloric acid, and other irrespirable gases, which is also caused by contact with the vocal cords, and which initiates the expulsive efforts in coughing—that this closure is nothing but a reflex action it is impossible to doubt. We have not therefore explained, however, that much-discussed disease, to which, amongst very numerous titles, the designations *asthma thymicum* and especially *spasmus glottidis* have been most widely applied. For this disease is characterised by the fact that paroxysms of spasm of the glottis appear in the absence of all the causes which usually set up reflex contraction of the glottis-closers. As an independent affection, laryngismus occurs exclusively during the age of childhood, while adults are liable only to hysterical attacks of glottis spasm. Of the children affected, the very great majority are rachitic, and in cases of true asthma thymicum, where I have had the opportunity of making post-mortem examinations, I have always found marked *hyperplasia of the thymus*, in one case of recent occurrence so considerable that it gave rise to atelectasis of extensive sections of the left lung. Nevertheless, good observers have repeatedly failed to detect this enlargement of the thymus. As for the larynx itself and the vagi, in particular the recurrent laryngeals, no definite and explanatory alterations have been observed, despite the most diligent search; rather, in uncomplicated cases, these parts have appeared quite normal. We have therefore at present no alternative but to assume the existence of an exalted irritability of the vagi, or at least of their laryngeal branches, a so-called *neurosis*, in the children affected—an assumption with which the often-observed hereditary predisposition of several members of the same family is in perfect accordance.

But whichever of these very different factors may be concerned, *the entrance of air will necessarily be impeded in consequence*, though in a very unequal degree, it is true. Some of these factors, *e.g.* a large foreign body impacted in the rima, a thick croupous membrane covering the vocal cords, a violent spasm of the glottis, a rectangular bend in the trachea, are of such a character that the air-stream is not simply obstructed, but absolutely arrested. Since, however, this involves nothing more or less than the complete cessation of respiration, I need hardly say that such an obstacle, if it persist even for a few minutes and no other entrance be opened for the air, must of necessity bring about *death by suffocation*. Not so when the windpipe is merely narrowed, not occluded; air now continues to enter the lungs, but in less than normal quantity, the amount being, *cæteris paribus*, small in proportion to the magnitude of the obstacle. True, one might be disposed to think that death by asphyxia could in this way be postponed, though not prevented,—supposing, that is, that each inspiration conveys a certain quantity less air into the lungs than is necessary to replace the air already respired. And yet individuals with a compressed trachea, a tumour of the larynx, or bilateral paralysis of the postici may live for weeks or months; even the majority of children who sicken with laryngeal croup pass happily through the disease without the necessity for tracheotomy; and if in a rabbit, or better still, a dog, you introduce into the trachea a cannula provided with a moveable cock, and then diminish the lumen so as to leave a very small aperture, the animal does not die during the next few hours or days. Rather the operation is followed by something of a very different nature, namely an essential *modification of respiration*. You see the rabbit at once begin to *breathe with effort*, the moment I, by a quarter-turn of the cock, reduce the lumen of the cannula to half; the nostrils expand strongly, the mouth is opened, the head thrown upwards and backwards, the spine straightened, and while previously you could only detect very slight movements of the flanks in the quietly breathing animal, you now observe very striking up and down movements of the thorax. All this may be the more easily noticed, *as the number of respirations is very considerably reduced*; the rabbit which, while it sat quiet and breathing freely, respired twenty-six times in a quarter-minute, now makes in the same space only twelve laboured respirations.

The breathing of human beings with stenosis of the larynx or trachea conforms completely to the foregoing type. The respirations are considerably reduced in number, they are effected with effort and labour, and by the aid of muscles which are not employed in ordinary free breathing; at the same time the passage of the air through the narrowed lumen gives rise to a hissing or sawing noise, often audible at a distance, which is termed *stridor* by the clinicians. The details of the picture differ, it is true, *according as inspiration or expiration or both together are impeded by the stenosis.* On fitting to the tracheal cannula of our rabbit a valve so constructed as to lie during inspiration in front of the external orifice of the free limb of the cannula, and to be easily thrown back during expiration, you at once see that the inspiration is prolonged and laboured in a high degree; the expiration, on the contrary, short and absolutely unattended with effort. But if the valve works in an opposite direction, constituting an obstacle to expiration while inspiration remains free, you notice a rapid and easy inspiration followed by a laboured and prolonged expiration. If, lastly, I diminish the lumen of the trachea by surrounding it with a wire ring so as to leave only a very narrow opening, the effort in each phase of respiration is equally intense. It is the same in human beings. If a polypus with a long pedicle or a flapping croupous membrane be situated beneath the glottis, and is thrown by the expirations against the under surface of the vocal cords, the easy and absolutely effortless inspiration is followed by a long and noisy expiration, in which the abdominal muscles contract energetically and the spinal column is bent forwards. An *inspiratory dyspnœa* is still more commonly observed in stenosis of the upper air-passage than this expiratory form; *e. g.* in ordinary cases of spasm of the glottis; when pedunculated polypi or croup membranes are situated above the glottis; in œdema glottidis, where the thick swellings formed by the aryteno-epiglottidean folds come to lie during inspiration in front of the rima; and especially in paralysis of the postici, in which the non-resisting vocal cords are in a sense sucked together by the inspiratory rarefaction of the air in the tubes, and the rima is still more narrowed than is usually the case under these circumstances. Here the expirations are short and noiseless, and the inspirations proportionately laboured. In addition to the ordinary inspiratory muscles—the diaphragm, the scaleni, and the intercostals—accessory muscles now come into action, first the serrati postici and levatores costarum, then the sterno-cleido-mastoids, pectorals, serrati antici, lastly the erector muscles of the spine, and when the stenosis is extreme the muscles extending from the trunk to the shoulder and arm ; prior to this the levatores alæ nasi, the sterno-thyroids, and sterno-hyoids have begun to contract. The alæ nasi dilate, the neck-muscles grow so tense that their contours are sharply defined, the larynx and trachea sink downwards, the spinal column is straightened out, the shoulders and arms firmly planted to secure the utmost possible enlargement of the thorax ; and these long continued, anxious, and torturing inspirations are accompanied by a loud hissing or whistling noise. At the height of the croup, or when the œdematous swelling of the aryteno-epiglottidean folds and region of the glottis has become so excessive that the expiratory stream cannot readily force the former asunder, inspiration and expiration are equally prolonged, forced, and noisy ; the same holds true when large foreign bodies become impacted in the rima ; and if in stenosis of the trachea due to cicatrices or to compression, the evidences of such striking and extreme dyspnœa do not usually appear, this is due to the fact that the obstructions so occasioned usually remain within moderate bounds. If, exceptionally, the encroachment on the space is considerable, the same stormy phenomena are present, and in particular one must here, as in all stenoses of the upper air-passage, be prepared for the fact that the ordinary symptoms will now and then be interrupted by very threatening paroxysms of dyspnœa.

There is no difficulty in explaining these remarkable alterations in the modus of respiration which so constantly and promptly set in on narrowing of the upper air-passage. When, in consequence of a considerable narrowing of the undivided section of the air-canal, the amount of air arriving in the lungs falls below the standard which is indispensable for the maintenance of the oxygen contents of the air in the alveoli at the amount necessary to regular respiration, the arterialisation of the blood cannot take place as usual, and blood enters the medulla poorer in oxygen and richer in carbonic acid, in a word more *venous*, than normal arterial blood. This venous blood, however, is a vigorous exciter of the respiratory centre, which responds to the stimulus thus produced by increased innervation of the respiratory nerves and muscles, *i. e.* by *dyspnœa*. The breathing is dyspnœic when the *number of respirations* taking place in the unit of time considerably exceeds the normal, and also when the single respirations are *deeper than usual and carried out with the help of accessory muscles;* still more will this be the case when both changes, augmented frequency and deepening of the respirations, occur simultaneously,—an effort, it is true, which the organism is not capable of making for an unlimited time. Which of these modes will be adopted in order to augment the respiratory movements, depends essentially on the cause exciting the dyspnœa, or on how far the nerves which control the rhythm of respiration are influenced by the latter. Here we are at once face to face with a mechanism of the greatest importance for the whole pathology of respiration, which has been termed by its discoverers Hering and Breuer,* the *"self-steering" of the respiration* by the vagus. In studying physiology, you have witnessed the elegant experiments by which it is demonstrated in the most striking way, that when the volume of the lung is augmented, expiratory stimuli reach the respiratory centre through the vagi, and that when the volume is diminished inspiratory stimuli are similarly carried; so that, if the vagi are intact, each expansion of the lung inhibits inspiration and furthers expiration, while, on the other hand, each diminution in bulk of the organ puts a stop to expiration and at once calls forth an inspiration. On this "self-steering" power depends the ordinary regular rhythm of our breathing; without it, inspiration would not follow directly, without any interval, on expiration, and without it, also, inspiration would not be succeeded by expiration long before the total inspiratory energy is used up. Unprovided with this mechanism, we should always breathe dyspnœically, as may in fact be observed in a rabbit both of whose vagi are divided. It is at once obvious, therefore, how important it is for respiration that the expansion or diminution of the lungs should proceed *without any impediment.* For if it be true that the expansion of the lungs puts a stop to inspiration, and their diminution to expiration, it follows logically that any obstacle to either phase must have the effect of *prolonging* it. Precisely this it is that is observed in the rabbit and also in human beings with narrowing of the upper air-passages; if the obstacle causes any difficulty of inspiration, the latter is extended and prolonged; if, on the contrary, the expulsion of air is impeded, the result is long drawn, laboured expirations. With the dyspnœa itself, *i. e.* the reaction of the respiratory centre, this change of rhythm of the respiratory movements has at bottom nothing to do; the prolongation of the particular respiratory phase appears at once on the establishment of the impediment, before any dyspnœa whatever has developed. In this reflex mechanism, however, must be sought the determining cause of the fact that *in stenoses of the upper air-passages the dyspnœa expresses itself in protracted and deepened, and hence less frequent respirations.*

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* Breuer, 'Wien. akad. Stzgsb.,' Bd. lviii, Abth. 2, Nov., 1868. Cf. Gad, 'A. f. Physiol.,' 1880, p. 1; Langendorff, ibid., 1879, Suppl., p. 48; J. Rosenthal, ibid., 1880, Suppl., p. 34, 1881, p. 39.

Here, too, as in so many other sections of our science, we observe mechanisms brought into action under pathological conditions which are calculated to diminish or even to compensate the disadvantages accruing from these conditions, and which we are therefore fully justified in terming "regulative." I have already stated that, in the absence of an increase of respiratory activity, the narrowing of the upper air-passages must rapidly lead to the extinction of respiration; and it is no less obvious that under such circumstances a simple increase of the frequency of the respirations would be of no service to the organism. It is necessary above all that a *prolongation* of the respirations should occur in order that as much air may pass the narrow aperture as usually enters by the physiological one, and next that the respirations should be *more vigorous* in order to overcome the impediment, the abnormal resistance. That an actual *regulation* of the disturbances produced by stenosis of the upper air-passages is brought about by the change described in the mode of respiration has been shown by H. Köhler, in an interesting series of experiments. Animals, the lumen of whose trachea he could at will diminish by means of a leaden wire placed around it, were caused to breathe from an air-receptacle resembling a spirometer, in which the air, as exhausted, was replaced by water flowing after it ; and, as the result, he found, without exception, that considerably more air was taken into the lungs with every prolonged and laboured inspiration than is ordinarily taken during the normal inspirations with the air-passages unobstructed. And this augmentation of the amount respired was so considerable that, in the unit of time, nearly as much air as in free respiration was breathed in by rabbits, and *a not inconsiderably greater quantity by cats and dogs.* Such being the state of affairs, it need excite no surprise that animals with a very considerable stenosis of the trachea may continue in excellent health for weeks, although their respiration is constantly dyspnœic and their demand for oxygen, owing to the forced respiratory movements, even exceeds that of animals breathing normally. This excess is just covered by their deepened inspirations, and so it comes about that the nutrition of the animals, their temperature and entire metabolism, are long maintained within perfectly normal limits. Determinations of the amount of air respired by human beings suffering from stenoses of the upper air-passages have not, so far as I know, been made as yet ; but such persons can evidently be no worse off in this respect than are the animals experimented on. At any rate many persons, the subjects of goitre, suffer for years from stenosis of the trachea without any prejudice to their other functions and nutrition, in spite of the persistent though moderate dyspnœa ; and when, as the result of bilateral paralysis of the postici, marked dyspnœa has developed, many months may pass during which the general state of the patient is fairly good. True, one point, which will shortly be discussed more thoroughly, must be taken into consideration here, namely *the varying amount of the oxygen-demand.* Such patients very soon learn to limit as far as possible their need for air, and while their condition is tolerable when all physical exertion is avoided and their habits are quiet and temperate in all respects, any departure from this mode of life easily brings about the danger that the respiratory apparatus may be no longer able to satisfy the excessive need for oxygen, in which case they pay for their imprudence by attacks of severe dyspnœa, often amounting to orthopnœa.

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* Köhler, 'A. f. exper. Pathol.,' vii, p. 1.

From the bifurcation of the trachea downwards, the conditions are more complicated. Above this point every factor which obstructs the passage at any particular spot must necessarily influence respiration through the whole extent of both lungs; but within the bronchial tree, one or even a large number of branches may be narrowed, or even fully occluded, without any prejudice whatever to the entrance of air into the remaining bronchi. For a pathological process occurring in the bronchi to have the effect of a stenosis of the trachea, it is necessary that all the tubes of the same united sectional area, or the greater number of them, should be affected. With such a process we are acquainted in *tetanic contraction of the small bronchi*, which, at least in very many instances, constitutes the cause of so-called *asthma bronchiale*. Whether this title is fairly applicable to everything at present included under it, is questionable enough, and I, at least, am not at all disposed to dispute that a tonic contraction of the diaphragm may be at the bottom of many of these attacks of asthma. But to completely deny for this reason, as Wintrich* and Bamberger† have done, the occurrence of spasm of the bronchi, I hold to be quite unjustifiable. The physiological possibility of a narrowing of the small and smallest bronchioles by the contraction of their muscles, which was held by many persons to be impossible on the evidence of inadequate experiments, cannot at present be disputed in the light of the exact and positive researches of L. Gerlach‡ and Mac Gillavry;§ moreover, the increase of pressure determined to occur, by these authors, in the trachea, owing to the contraction of the bronchioles on direct or reflex irritation of the vagi, was sufficiently great to make it necessary that we should not underestimate the amount of resistance thus occasioned. The paroxysms of dyspnœa which so often occur in old cases of emphysema, or in people with bronchial catarrh, are ordinarily caused, it is certain, by spasm of the bronchi, reflexly set up from the inflamed mucous membrane. But the typical paroxysms of true

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* Wintrich, in Virchow's 'Handb.,' v, i, p. 198.

† Bamberger, 'Würzb. med. Zeitschr.,' vi, Hft. 1, 2.

‡ L. Gerlach, 'Pflüg. A.,' xiii, p. 491, contains the older literature on this question.

§ Mac Gillavry, 'Arch. Néerland. d. sciences nat.,' xii, No. 5.

"essential" bronchial asthma, which is differentiated from the "symptomatic" form by the fact that, during the intervals between the paroxysms, the respiratory organs behave as in health, are also usually called forth in a reflex manner. The stimulus thereto may proceed from the most different organs possible, and need not be of any special character or intensity; on the contrary, the most remarkable feature of the malady is that numerous irritants, which in a normal subject would produce no effect whatever, give rise in the asthmatic to more or less violent paroxysms. It is hard to say on what this inreased excitability of the vagi depends, although the extremely frequent inheritance of bronchial asthma makes it likely enough that at least in these cases constitutional anomalies of congenital origin are at work. Since it was discovered by Leyden* that the sputum of the asthmatic almost constantly contains the same microscopic octahedra which, occurring in other localities, have long been known as Charcot's crystals (cf. vol. i, p. 489), the idea has been expressed that the presence of these pointed bodies in the bronchi may keep up a continuous irritation, with temporary exacerbations, of the nerve-terminations in the mucous membrane. To lay stress on the scanty sputum in which the crystals are expectorated towards the end of the paroxysm, and hence to pronounce the entire process to be a catarrhus acutissimus, as has been done by Traube† and quite recently by Fräntzel,‡ certainly appears to me to be scarcely justified. An inflammation which, although it may be a superficial one, extends in a few minutes over the entire air-passages, and in that time reaches its climax, is quite unknown in the rest of pathology; and if, during the paroxysm of asthma, a hyperæmic swelling of the bronchial mucous membrane accompanied by a secretion actually takes place, it is more natural to attribute this to a vaso-dilator neurosis associated with the spasm. The nature of the respiratory disturbance brought about by the bronchial spasm is, at any rate, not altered by the accompanying swelling; rather its original tendency is intensified by the swelling. I have already stated the manner in which the general spasm of the bronchi influences the respirations; it acts just as does stenosis of the trachea, but with one important difference, it is true. In stenosis of the trachea the narrowing is situated outside the thorax, but in bronchial spasm *within it*, and therefore within the area which is exposed to the pressure of the expiratory muscles. It follows from this, as explained by Biermer* with convincing clearness, that the increase of the expiratory pressure is very far from aiding in overcoming the obstacle in the bronchioles. Rather the same forced expiration which propels the air through the narrowed portion of the trachea is even capable of still further reducing the spasmodically contracted small bronchi, and can thus render them less pervious than before. But if this be so, both phases of respiration must be impeded by the bronchial spasm, yet expiration considerably more than inspiration. And so it happens in fact. During the asthmatic attack the inspirations are also, it is true, prolonged, laboured, and noisy, but this is true in a much higher degree of expiration, during which the patient, groaning loudly, attempts to reduce the cavity of the thorax by means of violent contractions of all the expiratory muscles. The resistance which the contracted bronchi oppose to the emptying of the alveoli is in fact so great that the diaphragm is unable to arch itself as usual, and remains throughout the whole attack at its low level.

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* Leyden, 'Virch. A.,' liv, p. 324.

† Traube, 'Ges. Abhandl.,' iii (Fränkel's edition), p. 616.

‡ Fräntzel, '(Neue) Charité-Annalen,' iv.

Such extreme dyspnœa occurs only exceptionally in *bronchitis*, whether the *simple catarrhal* form—one of the very commonest diseases, you are aware—or the much less frequent *fibrinous* or *croupous* variety, which is observed in connection with, or as a continuation downwards of, laryngeal croup; as an independent affection with the larynx intact; and, in a few cases, as the undoubted effect of the rupture of a softened caseous lymphatic gland into the trachea or a bronchus. The lumen of the bronchial tubes must, it is true, be reduced in every inflammation, firstly, by the swelling of the mucous membrane, and, secondly, by the accumulation of secretion or exudation in the tubes. Still the amount of narrowing varies greatly according to the calibre of the bronchi affected, the amount of secretion, and, still more, the ease or difficulty with which it is removed. A catarrh of the larger bronchi never constitutes an obstacle to respiration, and provided croup is confined to them, no danger arises to the respiratory function. On the other hand, an inflammation of the small and smallest bronchi is anything but a trifling affection, especially in children, whose air-tubes are normally narrow and whose muscular power is unequal to the task of expectorating the tenacious masses with sufficient rapidity from the tubes. This muscular feebleness is also in part the cause of the great danger attending capillary bronchitis in old and feeble individuals, as well as in patients who have passed through a long pyrexial attack. Unfortunately, also, we know only too well how many children affected with croup perish, after tracheotomy, from the croupous affection of the small bronchi. In such most severe cases of bronchitis, the dyspnœa may fully equal or even exceed that of the asthmatic, and it will resemble the dyspnœa of asthma also in this, that it is chiefly expiration that is impeded. Usually, however, as already stated, the dyspnœa of bronchitis is far from reaching such a pitch of severity, simply because the stenosis of the bronchi is only trifling; and in the great majority of cases the alteration of the respiratory type is confined to an *increase in frequency*, which must partly be ascribed to the pyrexia accompanying the bronchitis and partly to the irritation, due to the inflammation, of numerous sensitive terminations of the vagi in the bronchial mucous membrane. Since the well-known researches of Traube, we are aware that the vagus contains centripetal fibres *whose feeble stimulation increases the number of the respiratory movements*, while their strong irritation may even cause standstill of the breathing during inspiration. That other fibres having a different action pass in the vagus from the lungs to the medulla, has already been dwelt on, and we shall soon have to investigate this point more thoroughly; yet their existence cannot in any way tell against the foregoing interpretation of the increased frequency of the respirations in inflammatory diseases of the bronchi and pulmonary parenchyma.

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* Biermer, 'Volk. Vortr.,' No. 12.

Another circumstance contributes not a little to moderate the dyspnœa of the bronchitic, namely, that *all the bronchi are only rarely implicated*. As a rule, the middle and lower sections of the lungs are the seat of the bronchitis, while the bronchi of the upper portions escape altogether, or are much less affected. If, accordingly, bronchitis cannot, as ordinarily occurring, be placed amongst the processes which produce narrowing of all the branches of a united cross-section of the bronchial tree, this is still more true of a number of other factors which from their nature give rise to *purely local stenoses* of the bronchi. The simplest example is a *foreign body* which has entered the air-passages. This accident is most likely to occur, as is well known, when a person takes a deep inspiration, *e. g.* yawns, sighs, sobs, or the like, during a meal. The deeper the inspiration, the more liable will the foreign body be to pass straight into a bronchus, and as experience teaches, more frequently into the right than into the left. It may either become at once impacted in a branch bronchus, according to its size; or it may be transferred to a second branch by coughing, which forces it towards but not out through the larynx, and remain fixed in this branch—an occurrence that may even be repeated after a very long time has elapsed. If, as frequently happens, the bodies are round, they are wont from the first completely to occlude the lumen of the bronchus in which they have remained fixed; in the case of other bodies, *e.g.* dried peas, this does not occur till the peas have swelled; yet even angular and irregularly-shaped masses generally soon lead to complete occlusion, because their meshes and spaces become filled with bronchial secretion. Furthermore, tumours may, just as in the upper air-passages, produce local bronchial stenosis by compression from without or by growing into the lumen. In this way the lumen of one of the main bronchi may be reduced to a minute slit by an aneurysm of the aorta, or, much more rarely, of the pulmonary, by a tumour of the mediastinum, swollen bronchial glands, or epithelioma of the œsophagus; the same result is produced in the branch bronchi occupying the interior of the lungs, more especially by metastatic nodules in these organs. Such cancerous and sarcomatous nodules very frequently grow into a branch bronchus, just as does cancer of the œsophagus or of the bronchial glands into a main bronchus. Lastly, the new-formation may infiltrate the wall of the bronchus and in this way narrow its lumen, sometimes to a very considerable degree and for a long distance. This is a condition which is not infrequently observed in carcinosis and sarcomatosis, and was found especially in the remarkable disease of the *Schneeberg miners*, with which you are acquainted from a previous discussion (vol. ii, p. 743), and which was described by the local physicians as *cancer of the lung*, but proved histologically to have the characters of *lympho-sarcomatosis*. To the localised stenoses of the bronchi a very considerable contingent is contributed by *inflammatory* processes, other than the catarrhal and croupous bronchitis already discussed. These stenoses are due chiefly to the residua of inflammations, which take the form of *cicatrices*, *indurations*, *contracting bands of connective tissue*, and are found in the walls of the bronchi themselves, but much more frequently in the peribronchial and pulmonary tissue. The most ordinary causes of these interstitial cirrhotic processes are the diseases produced by the inhalation of dust, on which we shall shortly have to dwell more at length; syphilis may probably be made responsible for many of them; while some cicatrices of the bronchi must, it is evident, have originated in catarrhal and other ulcers. As the result of such indurative and cicatrising processes the complete obliteration of a bronchus may be brought about, and it appears to me not at all improbable that some of the cases described in the literature as *congenital imperviousness* of a bronchus should rather be regarded as acquired cicatricial occlusion of later origin. For dwarfing and imperviousness of bronchi are usually confined to monsters which are incapable of living; and in the interesting case, described by Ratjen,* of a man forty-nine years old who had an enormously hypertrophied right, and a very small completely atelectatic left, lung, the main bronchus of which was completely obliterated and converted into a solid connective tissue cord one and a half inches long, the discovery of tolerably abundant pigmentation of the atelectatic lung very obviously tells in favour of the belief that this lung must have performed its regular functions for a considerable time.

Let us now see what importance a narrowing or occlusion of one or more bronchi, in short, a local bronchial stenosis, possesses for respiration. It is true that the entrance of air to all the remaining tubes is, under such circumstances, quite free and unimpeded. Yet this is of little service. For, since the bronchi do not anywhere anastomose, air cannot be supplied from any other source to the alveolar territory of the affected bronchus. The alveoli are consequently lost to respiration, so long as the occlusion of the tube supplying them lasts; or, in other words, every local stenosis of a bronchus must necessarily cause a corresponding *diminution of the respiratory surface.* This is not to be disputed; and it is also indisputable that the organism can easily support such a loss, provided only it be moderate in degree. For the physiological respiratory surface, *i. e.* the surfaces of all the alveoli united, is extremely large; it is thus constituted from the first, to render it capable of meeting the greatest and most sudden demands for oxygen, and, as you are aware, all the alveoli are very far from being equally and strongly called upon in ordinary respiration. While, then, the insignificance of single stenoses of the bronchi is apparent from the foregoing, the prejudicial effects of occlusion of larger bronchial territories are partly met by the intentional or instinctive limitation of the demand for oxygen, already referred to. This implies, however, that there are bounds, beyond which *the local stenoses of the bronchi are also productive of breathlessness and dyspnœic breathing.* In many cases, especially of mere narrowing of bronchi, the dyspnœa is besides the simplest and most advantageous means of regulation, in that the deep inspirations and forced expirations are capable of overcoming obstacles which the ordinary respirations are unable to conquer. Not so, however, when the affected bronchi are completely occluded and the strong respiratory movements fail to open them.

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* Ratjen, 'Virch. A.,' xxxviii, p. 172.

The first and immediate result of the closure of a larger bronchial territory is the unnatural distension or, as this is termed, *the inflation of the pervious sections of the lungs.* For if the thorax be more strongly distended than usual by the dyspnœic, and therefore deeper, respirations, while large portions of lung cannot increase in volume owing to the occlusion of the bronchi, the entire force of the inspiratory pull must necessarily act on those sections of the lungs which are accessible to air, in so far as these are capable of yielding.

Such a considerable compensatory inflation may, in fact, be brought about in this way as to *endanger life* itself. At any rate, Lichtheim* has repeatedly found that rabbits, in which he had firmly plugged one of the main bronchi by a laminaria tent introduced from the trachea, survived the operation a short time only. In a number of these animals, the inflation of the other lung was so considerable as to cause its *rupture*, and the resulting pneumothorax had terminated respiration acutely. Some of the animals, however, perished without pneumothorax within twenty-four hours, clearly because, the pulmonary capillaries being overstretched, they could not with their impeded circulation adequately minister to the exchange of gases. That the cause of death must be sought in this and no other factor is best shown by the comparative harmlessness of occlusion of one of the main bronchi when the corresponding pleural cavity is opened. Ligature of the left bronchus from the pleural cavity—whereupon the cause of the excessive distension of the right lung ceases to exist—was well borne by Lichtheim's rabbits, which died only after some weeks in consequence of a scarcely avoidable purulent pleuritis.

Such an extreme and threatening degree of inflation of the pervious portions of the lungs, arises only when a very large bronchial territory is blocked and the blocking occurs suddenly. In Lichtheim's experiments, when the tent lay a little lower down than usual so that the branch to the superior lobe remained free, this lobe participated to a marked degree in the inflation, while the other lung was much less distended than after complete occlusion of the main bronchus; the animals then lived for weeks without any dyspnœa worth mentioning. On the other hand, in Ratjen's case, to which reference has just been made, the right lung was enormously enlarged, so that its upper and middle lobes, more especially, filled up the greater part of the left half of the thorax; still the diameter of the alveoli was perfectly normal, and there was not the least evidence of dilatation, such as is characteristic of the inflated lung. A *true compensatory hypertrophy* had developed, and not a compensatory inflation, because, owing to the gradual extinction of respiration in the left lung, the circulation through it became less and less copious, while *pari passu* the more abundant supply to the other lung afforded the means of an actual increase of growth. As a matter of fact, the hypertrophied lung had so well performed its function, that its possessor had never had any reason to complain of his respiratory organs during the whole forty-nine years of his life. I just now stated, with regard to the rabbit, that in acute occlusion of the bronchi, the second lung only then becomes considerably inflated, when the main bronchus or all the middle-sized tubes are impervious. In the human being, too, when the obstacle is seated in some of the bronchi only, the abnormal dilatation is, as a rule, confined to the neighbouring parts of the same lung. This condition, which is, properly speaking, a greater *unfolding* of single sections of the lung, is of very common occurrence, and innumerable opportunities are presented for observing it, especially at the anterior borders. Though the condition is often called vicarious emphysema, this is, in my opinion, an erroneous expression. True emphysema involves the presence of defects in the alveolar septa, so that alveoli which were originally distinct coalesce to form more or less capacious air-sacs; and it is by no means established, though frequently assumed, that actual emphysema can arise from simple dilatation of the alveoli with the bronchi pervious. Usually, in those portions of the lung which are pervious and not otherwise altered pathologically, only the very finest bronchioles with thin and yielding walls take part in the compensatory dilatation; the larger bronchi escape, provided no conditions be present to prevent that degree of alveolar dilatation which is necessary to fill out the thorax. True, it happens fairly often that the bronchi of medium size are found dilated behind a stenosis of the fine bronchioles—the effect, no doubt, of the permanent inspiratory pull, to which they more readily succumb when their walls have atrophied from chronic catarrh.

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* Lichtheim, 'A. f. exper. Pathol.,' x, p. 54.

The effects exerted by a local stenosis of the bronchi on the portions of lung lying *beyond* it, are also far from always the same. The matter is simplest when a bronchus is *totally* occluded; for the certain and inevitable result then is, that the section of lung supplied by it becomes *in a short time* *completely emptied of air.* That this fœtal condition, or, as it is usually termed, *atelectasis*, always follows the closure of the afferent bronchi has long been known, and several decades ago was experimentally demonstrated by Traube;* yet full clearness as to the connection of the events taking place here was only very recently arrived at through Lichtheim's† very interesting research, to which reference has repeatedly been made. As the result of Lichtheim's experiments what was previously at most a guess has been converted into a certainty, and we now know that when atmospheric air is prevented from entering a section of the lung, *the air within it at once commences to be absorbed by the circulating blood.* The oxygen, which is taken up by the blood independently of the partial pressure, is the first to disappear; the carbonic acid follows next; and lastly, owing to its low coefficient of absorption, the nitrogen. But, rapidly or slowly, the mixture of gases finally disappears to the last vestige, because the elasticity of the pulmonary parenchyma is not satisfied till the last bubble of air is expelled. This is rendered possible with the thorax closed by the vicarious dilatation, already discussed, of the alveoli occupying the pervious sections of the lung; for, by the aid of the dilatation, the elastic force of the pulmonary tissue can make itself fully felt, and reduce the volume of the lung *pari passu* with the absorption of gas so that the tension of the confined air never falls below the measure which is indispensable to the progress of absorption.

This completely airless, but otherwise unaltered, condition of a section of the lung may persist just as long as the occlusion of the bronchus distributed to it lasts; and an opportunity often presents itself of observing such circumscribed atelectases in the bodies of persons whose bronchi are plugged by inflammatory—catarrhal, or croupous—exudation. Yet it is not always so. An atelectatic section of the lung is, it is true, completely lost to respiration, yet the circulation, though no longer completely regular, always continues in it, so that, consequently, transudative and exudative processes may take place therein; while the small bronchi, whose circulation suffers still less, need not cease secreting. If now abundant secretion and exudation occur—and these may be the result of many kinds of bronchial stenosis, such as occlusion by organic, decomposable foreign bodies or by masses of inspissated bronchial secretion—and the newly produced materials go on accumulating in the spaces of the isolated portions of the lung, a permanent and very considerable *ectasis* of the over-filled bronchi may be set up. That *a true bronchiectasis* may thus originate in advance of an occlusion of a bronchus has, it is true, been pronounced improbable by many; but anyone who has ever seen how, after Lichtheim's occlusion of the main bronchus, the lung becomes converted into a cellular sac containing pus, precisely after the manner of a pyonephrosis, can no longer entertain any doubt on this point.

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* Traube, 'Ges. Abhandl.,' i, p. 1.

† Lichtheim, 'A. f. exper. Pathol.,' x, p. 54.

Atelectasis and its sequelæ do not result when the bronchi distributed to the affected sections of the lung are only *narrowed* and not completely impervious. True, the individual circumstances of the case must be taken into account here also, since the same obstacle which in a vigorous man allows the entrance of the inspiratory stream, cannot be overcome by the muscles of feeble individuals, *e. g.* children and old people and persons exhausted by pyrexia. Provided, however, that the obstacle causes, in the individual affected, not an occlusion but only a stenosis of one or more bronchi, each deep inspiration at least, will convey a quantity of air into the alveoli lying beyond the stenosed spot; and if now, from any cause, the expiration is not forced in the same degree as the inspiration, it may easily happen that less air will be expelled through the narrowed passage than entered by it, with the result that there is developed a marked ectasis of the alveoli, or, as Niemeyer terms it, a *permanent inspiratory expansion* of them. But in addition to this really very common appearance, true emphysema with rarefaction of the alveolar walls is met with very often in advance of a bronchial stenosis; but for its explanation the theory of Laennec just referred to is quite inadequate. To explain it one must rather turn to *the forced expirations.* I remind you in particular of the remark already made with regard to the effect of increased expiratory pressure on the small bronchi. For if the small bronchi are compressed by an abnormally high expiratory pressure, it is very easy to understand that a simple narrowing should be converted during expiration into an occlusion, when the compressed air of the alveoli could no longer escape through its regular outlets. The result will be *rupture of the alveola septa* and the establishment of *emphysema,* either the ordinary *vesicular* variety, or, in extreme cases, the *interstitial,* where the air of the alveoli enters the interlobular septa, the subpleural tissues, &c. As is evident without further explanation, it is more particularly *stenosis of the small bronchi that occasions emphysema;* and you will consequently not be surprised to hear that both bronchial asthma and *catarrhe sec*—*i. e.* catarrhal inflammation of the middle and small bronchi with a tenacious secretion that is difficult to expectorate—frequently pass on, as it is called, into emphysema. When the large bronchi are narrowed, on the other hand, these same conditions lead less to emphysema than to dilatation of the bronchial ramifications. How much the paroxysms of coughing inseparable from bronchitis further the process now under discussion we shall later on have to consider.

When the air has passed the bronchi, its access to the surface of the pulmonary capillaries may be prevented in the *alveoli* themselves. As a rule it will be absolutely prevented, because, owing to the minute size of the alveoli, any impediment there arising usually becomes an absolute one. True, the dilatation and arching inwards of the pulmonary capillaries into the alveoli, such as characterise so-called *brown induration* of the lungs in cardiac lesions, especially of the mitral orifice, might, with Traube,* be regarded as an encroachment upon the alveolar spaces—though it is questionable whether this is really the cause of the difficult breathing of these patients. At any rate, brown induration, in which we have to deal with a narrowing and not with an occlusion of the alveoli, is the only affection which, while involving the pulmonary vessels collectively, may yet be tolerated for a long period: this would obviously be impossible in a really general *occlusion* of the alveoli. In this lies the extreme *danger of general œdema of the lung, i. e.* **the saturation of the** pulmonary alveoli with liquid. On a former occasion (vol. i, p. 522, *et seq.*) I spoke at some length of general pulmonary œdema, and I then explained that it is simply an *œdema of stagnation*, depending on *paralysis of the left ventricle while the right continues to contract.* The name applied to this general œdema by the ancients and more recently again by Traube—*pneumonia serosa*—is decidedly false, and I am the more inclined to advise against its employment, as *a true inflammatory œdema of the lung* actually occurs. We speak of inflammatory œdema of the lung, as of all other organs, when an inflammation has not gone further than the exudation of a watery fluid; when, that is, the exudation is neither rich in cells nor coagulated. Hence we meet it most regularly at the commencement of a true croupous pneumonia, when a special name, *engouement*, is customary; and, secondly, as an indication of the extension of the pneumonic process, in the immediate vicinity of the hepatised portions. From the nature of the case, this inflammatory œdema is never general, but always circumscribed, and often indeed limited to small portions of the lung. In its significance for the respiration, therefore, it cannot approximately vie with the general form, and falls completely into the shade when associated with advanced degrees of inflammation, and especially hepatisation. Its subordination is the more distinct, since the alveoli are rendered decidedly more inaccessible to air by filling with a markedly inflammatory *infiltration* than by the mere œdema. It is here immaterial whether the infiltration be a *croupous*, *catarrhal*, *gelatinous*, or *caseous* one; the implicated alveoli are always useless to respiration, and in this regard the most important consideration is, how many pulmonary vesicles are cut off, *i. e.* what is the extent of the inflammation. If, for example, a catarrhal or a caseous infiltration involves a great number of lobules in both lungs, it may constitute a greater impediment to respiration than an ordinary croupous pneumonia; though, in most cases, the croupous form gives rise to more respiratory disturbance, owing to the greater rapidity with which it causes complete occlusion of the affected portions of the lungs.

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* 'Ges. Abhandl.,' ii, 308.

As regards the imperviousness to air, it is a matter of indifference whether the [illegible] filled with an inflammatory infiltration, or with the fluid or solid products of any other pathological process. Here may be cited the plugging of the air-vesicles with blood extravasated *per diapedesin* in *hæmoptoic* or *hæmorrhagic infarct ;* but here, it is true, the section of lung involved is already worthless as far as respiration is concerned, since the regular circulation through it has ceased. For this reason, a hæmorrhagic infarct is of more importance for respiration than is a *pulmonary hæmorrhage per rhexin*, or, as this is also called, an *apoplexia pulmonis.* Provided, of course, their size is the same ; for I need hardly say that a person into whose trachea, *e. g.*, an aortic or subclavian aneurysm bursts, must die asphyxiated ; while the loss of a few grams of blood into the pulmonary tissue is a trifling accident to respiration, since, as you will shortly hear, so small a quantity of fresh blood very rapidly disappears by absorption from the alveoli into which it has been aspirated. Less extensive, and therefore without any significance from our present standpoint, are *mycotic* foci in the lungs, *i. e.* the filling of alveoli with true *fungi ;* they are, moreover, of extremely rare occurrence. The more importance attaches to the *rôle* played by *tumour-forming processes* in the lungs, by reason both of their extreme frequency and the wide distribution and bulk attained by them. Chief amongst them is *tuberculosis,* whose classical seat is precisely the lungs ; and, secondly, the true *tumours,* which though rare as primary growths, all the more frequently select the lungs in metastatic form. As regards the question now engaging our attention, it is here again quiet immaterial what the structure of the tumours is, where they originate, and what the character of their growth ; and it would amount to mere hair-splitting did we seek to distinguish whether the masses render the alveoli impervious by penetrating them or by compressing them from without. For the alveoli being so small, both modes will certainly go hand in hand, at least in all metastatic tumours and in the infective granulomata—that is, in the great majority of all new growths ; and it is in any case undoubted that the pulmonary vesicles are lost to respiration within the limits of the tumours.

In the *interstitial, indurative* and *cirrhotic processes,* so extremely common in the lungs, it is only rarely that we can discover whether the destruction of the vesicles by alveolar pneumonia has preceded the increase of the interstitial tissue, or whether, conversely, the latter has brought about the disappearance of the alveoli by compression and consecutive contraction; here too we shall probably come nearest the truth if we admit the action of both factors. There are, however, a number of processes which render a larger or smaller number of vesicles impervious to air only and solely by *compression from without*. In this category several forms of bronchiectasis must be placed. For whether the dilatation involves the smaller or larger bronchi, whether it affects the upper or the lower lobe, whether it originates rapidly or slowly, it can never occur in the closed thorax except at the expense of other parts, which have previously occupied the space by which the ectatic bronchi now exceed their former normal volume; the parts most readily offering themselves are the alveoli. Now, in some cases of bronchiectasis, the destruction of the alveoli precedes the dilatation of the bronchi, as when the condition is developed beyond the obliteration of a bronchial tube, or when the by no means uncommon form is present, whose cause has correctly been sought since Corrigan's time, in the extra-bronchial pull of cirrhotic pulmonary tissue. But besides these, typical and far from inconsiderable bronchiectases occur, whose mode of origin is not explainable by reference to such processes. We have then to deal almost exclusively with the subjects of *chronic bronchial catarrh*, and hence it is at any rate an obvious idea to attribute the bronchiectases, on the one hand, to the atony, loss of elasticity, and failure of contractile power of the bronchial walls brought about by the chronic inflammation; and, on the other hand, to the continuous increase of the expiratory pressure, especially intense during the paroxysms of coughing. It was these, so to speak, primary bronchiectases I had chiefly in mind, when I thought it necessary to cite this condition as one of the factors which shut off the alveoli from the air by external pressure. But still more wide-spread, and consequently more striking, effects attend compression by *large tumours* inside the thorax, by copious *pleuritic exudations*, and by *accumulations of gas* in the pleural cavities under a tension exceeding that of the atmosphere. That we have by no means always to deal with compression of the lung, when in cases of pleuritic exudation, pneumothorax, pericardial effusion, or enlargement of the heart, a more or less large number of alveoli are found to be airless, you will presently learn; but when, in such conditions, the greater part of the blood even is dislodged from the pulmonary vessels, and the lung is converted into a flattened cake, with a volume much less than that of the normal airless organ, it is impossible to doubt that an actual compression has here been at work.

The processes just discussed do not, however, exhaust the possible derangements which may in the alveoli oppose the entrance of air and its interchange with the gases of the pulmonary capillaries. In all other sections of the air-passages the channel was perfectly free and unobstructed, provided the lumen of the tube concerned was not reduced by causes acting within it or from without. It is not so, however, in the alveoli, for, unlike the larger air-passages and to a less extent the bronchioles, the *volume* of the alveoli is *not constant.* At the height of inspiration and the end of expiration the size of the air-vesicles differs greatly. In other words, if the interchange of gases, that is, respiration, is to proceed regularly, the alveoli must be capable *of freely expanding during inspiration and of collapsing with no less freedom during expiration.* But obstacles interfering with either phase are by no means rare. Here must be mentioned, in the first place, *the adhesion of the two layers of the pleura,* the importance of which for respiration was first pointed out by Donders in an essay* often quoted. In a normal condition, the lungs increase in volume not only in their transverse and antero-posterior diameters, but vertically; they glide along the walls of the thorax in the direction from above downwards and from behind forwards in such a way that the apices and posterior borders remain fixed, and participate least in the change of position. Each alveolus moves along the thoracic wall for a distance equal to the total longitudinal dilatation of all the pulmonary vesicles situated above it, and thus the amount of displacement of the inferior borders of the lung may be regarded as the measure of the expansion of the alveoli collectively. If the lungs are fixed to the parietes by firm adhesions, which cannot be stretched at all or only with difficulty, the displacement of the organs will necessarily be interfered with; and the obstacle will be least if the synechia implicates merely the apex and posterior borders, and greatest if the adhesion be situated over the lowermost sections. Under these circumstances a more or less large number of alveoli will fail to expand during inspiration to the normal extent, and though air may enter them, it will be less than normal in amount.

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* Donders, 'Zeitschr. f. rat. Medicin,' N. F. iii, p. 39.

A much more serious condition is produced by the establishment of a *free communication between the pleural cavity and the atmospheric air*. This may be due to a perforating wound or a fistula of the wall of the thorax; to the rupture of a phthisical or bronchiectatic cavity, an abscess, a focus of gangrene, an emphysematous vesicle—in short, of any necrotic or greatly attenuated portion of the surface of the lung and pleura; and in rare cases to perforation of ulcers of the œsophagus, or of gastric ulcers, after antecedent adhesion to the diaphragm. Rupture proceeding from the lung —by far the commonest cause of pneumothorax—may sometimes take place quite suddenly in consequence of a forced inspiration or expiration, *e. g.* a fit of coughing; but, as a rule, it develops slowly as the result of one of the ulcerative or necrotic processes already mentioned, though then too the perforation proper occurs suddenly, in a moment. Now whatever be the cause of such a pneumothorax, *i. e.* of one freely communicating with the atmosphere, or more briefly *open*, the accident will always be attended by serious consequences for the respiration on the affected side of the thorax. For the lung henceforward will no longer follow the inspiratory pull of the chest-wall, and though the air-passages are perfectly free, *no air will enter the lung*. This point being arrived at, no long time will elapse before the alveoli rid themselves of the air contained in them at the commencement of the pneumothorax; the lung becomes *atelectatic*. For the elasticity of the lung is now free to assert itself without hindrance, till the last bubble of air is taken up from the alveoli by the circulating blood, and the lung is reduced to its natural volume, or, if you prefer it, to the volume natural to it before respiration began, *i. e.* in a fœtal condition. We have in the foregoing assumed that the lung is freely moveable, and that no synechia of the pleura is present. Should this not be the case, and the lung be adherent over a smaller or larger area to the wall of the thorax, the pneumothorax, though open, will be *saccular*. The atelectasis will then always be incomplete, since the elasticity of the lung is incapable of overcoming the resistance offered by the firm adhesions.

All this has reference, as stated, to pneumothorax with a free communication between the pleural cavity and the atmosphere. It does not apply to *closed* pneumothorax, when, for example, the aperture in the thorax is united or the perforation of the lung occluded by a layer of fibrin. For when a certain amount of air is present in the pleural cavity, and does not vary with inspiration or expiration, breathing is not prevented in consequence—indeed, it is in reality no more impeded than if an equal volume of liquids or solids were present there. Only when the intra-pleural air has acquired *an abnormally high tension,* does the closed pneumothorax prove highly detrimental to the affected lung. The tension is increased when the opening by which the pleural cavity communicates with the atmosphere is so shaped as to admit air during inspiration and to prevent its escape during expiration. Such an aperture is not exactly rare in the commonest form of pneumothorax, namely, the phthisical, where, owing to its peculiarly jagged outline, it acts precisely like a valve, opening on inspiration and closing on expiration, and with greater certainty, too, the higher the tension already acquired by the intra-pleural air. This movement continues till finally the tension of the air in the pleural cavity has become so considerable that no more can enter during inspiration, and the valve remains permanently closed. This *valvular pneumothorax,* as it is termed,* accordingly forms in a measure a subvariety of closed pneumothorax; but its characteristic feature is the great tension of the air present in the pleural cavity. In consequence of this, the affected half of the thorax is expanded even beyond the limits of the deepest inspiration, while the lung, on the contrary, is not merely airless but completely *compressed,* and lies against the spinal column as a flattened cake, reduced to the least possible volume. The danger of this condition is enhanced by the fact that it may only too easily become permanent; for if, shortly after it has originated, the intra-pleural air be removed either by puncture or by absorption, the valve again commences to act in the manner already described; and furthermore, the air fails to be absorbed or is removed with difficulty when the pneumothorax, as almost always happens, becomes associated with a fibrino-serous, or still more frequently a fibrino-purulent, pleuritis, which in some cases precedes the pneumothorax and in the remaining ones follows sooner or later,* but always in a comparatively short time. There need be no fear of such pernicious consequences, however, when, as fortunately occurs in many cases, the tension of the air in the closed pneumothorax is slight; rather, as already noticed, we may then regard its mechanical influence on respiration as equivalent to that which would be exerted by a corresponding accumulation of liquid in the pleural cavity.

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* Cf. Weil, 'D. A. f. klin. Med.,' xxv, p. 1, xxix, p. 364.

The nature of this influence is taught us, not only by experiment, but by too frequent clinical and anatomical experience. For purposes of experiment it is not advisable to inject air into the pleura of a rabbit, owing to the rapidity with which it is absorbed; the same objection applies to watery indifferent fluids such as salt solution, so that it will be best to employ an oily fluid, *e. g.* pure *olive oil.* As Wiener† recently showed in the laboratory here, the oil is also absorbed in considerable quantities from the pleural cavity, and then gives rise to enormous fatty embolism, chiefly of the lung, but also of all the remaining organs; still a tolerably long time is required for its absorption, and if the oil be pure and undecomposed it is followed by no local or general prejudice to the organism. If, then, the lung is examined when absorption is not far advanced, *i. e.* some hours or even one to two days after injection, one may be certain of determining the purely mechanical effects of this pleural accumulation of fluid upon the organ. Similar opportunities are presented in human pathology; first, by pleuritic *transudations* and *exudations* of moderate dimensions; and second, by numerous other processes by which the cavity of the thorax is encroached upon unilaterally or bilaterally, as *e.g.* large tumours occupying the interior of the cavity, whether growing into it from the chest-wall or diaphragm, or originating within it, like *aortic aneurysms, substernal goitres, hypertrophies of the thymus,* and mediastinal tumours: large *pericardial exudations,* and even *excentric hypertrophies of the heart* must also be placed here. But the most considerable, and hence most important encroachments on the thoracic cavity are occasioned by the *forcing upwards of the diaphragm,* which itself may be due to large abdominal tumours, a bulky ascites, or—probably the most frequent cause—extreme meteorism. Lastly, *deformities* of the thorax play an important *rôle,* especially the very common *kyphoskoliosis,* in which that half of the thorax at least, towards which the convexity of the spinal curvature is directed, may occasionally be very considerably reduced.

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* Senator, 'Ztsch. f. klin. Med.,' ii, Hft. 2.

† Wiener, 'A. f. exper. Pathol.,' xi, p. 275.

The consequence of every reduction in size of the thoracic cavity, however conditioned, may evidently be defined to consist in the inability of the implicated lung to expand in the same manner as under physiological conditions, since it cannot take possession of the entire space procured by the inspiratory enlargement of the thorax. This latter quantity is not, it is true, constant; on a deep inspiration it is much more considerable than on a shallow one; and it is accordingly evident that a deep inspiration will at least partially compensate the prejudicial influence of a factor circumscribing the cavity. If, for example, there be present in a pleural cavity a moderate amount, about 200 to 300 grams, transudation, the volume of the lung will undoubtedly be no less great after a deep inspiration than it would be after an ordinary easy inspiration, were no transudation present. But no one, you are aware, continues long to voluntarily carry out forced and laboured inspirations, for this occurs only under the influence of dyspnœa. A glance at the rabbit, however, into whose right pleural cavity I have just injected 10 c.cm. oil —certainly a considerable quantity for this animal—shows that it has no dyspnœa whatever; it breathes a little oftener than before the injection, but without any muscular effort. Still less does dyspnœa occur in human beings with an ordinary pleural transudation which is only slowly and gradually poured out, or in a person with kyphoskoliosis, provided he suffers from no respiratory disease. But if, under such circumstances, compensation by a dyspnœic deepening of the respirations does not usually take place, it becomes the more necessary to inquire, How does the lung behave? In the first place, it is theoretically conceivable that the action of the space-reducing factor may be distributed equally over all the alveoli of the affected lung, in such a way that each single alveolus remains smaller by the amount obtained through dividing the volume of the factor in question by the total number of pulmonary vesicles. Still nature does not so proceed. The action of the space-reducing factor, as is easily understood in an organ having the structure of the lung, extends solely to the portions of lung in its immediate proximity; their expansion is prevented, and the entrance of air into them is consequently impossible. But this, you know, is the signal for the immediate absorption of the air present in the alveoli, and you will not be surprised to learn that the result of all these space-reducing factors is *partial atelectasis*. The extent of the atelectasis depends exclusively on the amount of space lost, and its situation is determined, as already indicated, by the locality of the factor in question. Thus in pleuritic transudations and exudations the posterior and inferior portions of the lung become atelectatic; in meteorism, the base of the lung; in pericardial exudations, chiefly the inner portion of the left lung; in mediastinal tumours, the anterior borders; in goitre and in hypertrophy of the thymus, the anterior parts of both superior lobes. The tissue involved is brownish red, flabby, and tough, smooth and comparatively dry on section, and though easily inflated from the bronchus, is completely airless—in a word, *atelectatic.*

We have lastly to consider another circumstance which practically may be very important, *the incapacity of the lung to expand in regular fashion,* although no evident gross impediment is present either in the bronchi or alveoli. Such a condition is not rarely met with in a lung which has for a considerable time been compressed by a large pleuritic exudation, and also appears to occur in sections of lung which have long been atelectatic. The cause of the inability to expand has not been satisfactorily cleared up. That a weakening of the elasticity of the lung, which we shall presently have to discuss more minutely, is partially responsible, there can be no doubt; yet still more importance apparently attaches to the fact that the walls of the bronchioles and alveoli adhere firmly and are in a measure glued together, in consequence of their prolonged immediate contact. Possibly this condition is preceded by a loss of epithelium, which in the compressed lung at any rate might be looked upon as the result of an inadequate circulation. An actual mass of material, filling the air-passages, is certainly not found in the affected lung.

Not only must the alveoli, we said, expand properly during inspiration, but they must be *capable of adequately contracting during expiration.* But if you bear in mind that in ordinary quiet breathing with the thorax normal, it is solely the elasticity of the pulmonary tissue that causes the diminution of the alveoli, it will at once be apparent that *every considerable reduction of elasticity must prejudice* the expiratory contraction of the alveoli, and consequently the entrance of air during the succeeding inspiration—must interfere, in fact, with the *exchange of gases* generally. Now I have mentioned already—and it will not seem particularly remarkable to you—that strong compression as well as the abnormal vicarious inflation of the lung each exerts an injurious effect on the elasticity of the organ, especially if developing rapidly and lasting long. But it would appear that many diseased conditions, which *per se* have little connection with the lungs, are by no means without influence on the elasticity of these organs. At any rate Perls,* on measuring, according to the method of Donders, by a tracheal manometer, the amount of retraction of the lung occurring after opening the pleural cavity in cases of typhoid fever and acute phosphorus poisoning, found very low figures, but no local disease of the lung to account for them, a result which seems all the more remarkable, as he failed to meet it in other acute general diseases, *e. g.* in typhus and septicæmia. Hence it is possible that *individual* differences in the amount of elasticity were in question, especially as such differences may here be very great. As regards that disease in particular, in which the deficient elasticity of the pulmonary tissue forms the central point of all the pathological phenomena, it may be looked upon as established that, in a great number of cases at least, the deficiency *depends on a congenital imperfection and inadequate development of the elastic tissue of the lungs.** I refer to that extremely common affection, which is usually termed both by the public and by physicians, *pulmonary emphysema*, though we shall, with Traube, more correctly call it *volumen pulmonum auctum.* It is, at any rate, to this condition that the usual description of the symptoms of emphysema applies, the barrel-shaped thorax, the low level of the diaphragm, the slight præcordial dulness, &c.; and it is this affection that is so prone to be inherited in certain families, and to give rise even in the children to the most severe disturbances of respiration. Since, however, this change usually involves the whole of both lungs, the simple increase in volume, or false emphysema, is generally much more important pathologically than is *the true emphysema of the pathological anatomist.* For this latter affection, which is characterised by defects in, and the disappearance of, alveolar septa, and the consecutive union of several pulmonary vesicles to form more or less large air-sacs, is usually limited to circumscribed portions of the lung, while the rest of the pulmonary parenchyma is normal in constitution and performs its functions normally. In those very rare cases, it is true, in which the emphysema implicates all the lobes, and converts both lungs into a system of thin-walled air-sacs, it is obvious, without further proof, that the expiratory contraction must if possible be still more difficult than in the large lungs with a defective development of elastic tissue.

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* Perls, 'D. A. f. klin. Med.,' vi, p. 1.

There are, as you perceive, a great many possible impediments to the entrance and renewal of air in the alveoli. But whether the pulmonary vesicles are filled with solid or with fluid materials, whether they are compressed or atelectatic, whether their inspiratory expansion or their expiratory contraction is interfered with, the immediate result, so far as respiration is concerned, must invariably amount to a *loss.* For the alveoli whose change of volume is opposed by obstacles will either take a smaller share than normal in the respiratory interchange of gases, or if fully occluded will not participate in it at all. If, however, the exclusion of some of the bronchi is unattended by damage to the organism, this will, it is evident, no less be the case when a few alveoli are lost to respiration: more especially if the body be kept in repose, *i. e.* if the demand for oxygen be slight, the loss even of extensive groups of alveoli will not be followed by any respiratory disturbance or injury to the patient's general condition. And it will appear no less plausible to you that the organism should more successfully accommodate itself to the diminished respiratory surface, the more slowly the diminution takes place. It is for this reason that, as already pointed out, persons affected with kyphoskoliosis or with extensive pleuritic adhesions are usually quite free from dyspnœa; and physical examination often enough reveals the presence of very considerable pleuritic transudation or of evident condensation of the parenchyma, though the patient's mode of respiration would not point to anything abnormal in the thorax. On the other hand, the organism reacts more energetically to an extensive loss of alveoli in proportion as this takes place rapidly. Hence it is that acute œdema of the lungs gives rise to such stormy symptoms, and that pneumothorax has a similar effect when involving a lung which till then had respired normally; for if the lung from which air has escaped into the pleural cavity is extensively infiltrated or its density otherwise increased, or if it contains a number of large cavities, as often happens in the phthisical, the pneumothorax may occur without being noticed and almost without symptoms. An inflammatory infiltration developing in a very short time in croupous pneumonia will be much worse borne than will an equally large but more slowly developed caseous or gelatinous infiltration; and that the dyspnœa in acute miliary tuberculosis is invariably strikingly in excess of that occurring in chronic tuberculosis, even when the amount of chronic condensation does not fall short of the sum-total of the acute nodules, this too depends in a great measure on the acuteness of the process. There is present, it is true, in many of these diseases an additional factor, which interferes with the accommodation, and hence with the correction of the evil, namely the *pyrexia*. For the pyrexia, by increasing, on the one hand, the production of carbonic acid, and, on the other, the frequency of the pulse and respirations, and thus augmenting the muscular work done by the individual, causes a decidedly greater demand for oxygen, and thus gives increased importance to any diminution of the respiratory surface. In fact, the importance of pyrexia as regards the question now engaging our attention is taught by the circumstance that respiration is much less hampered by cancerous or sarcomatous nodules than by equally extensive inflammatory infiltrations, and is more especially shown by the state of pneumonic patients before and after the crisis; for though so far the infiltration has not been altered, the same patient who, up to the crisis, presented the most marked dyspnœa, now breathes much more quietly, indeed, almost as in health.

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* Cf. Eppinger, 'Prag. Vierteljahrsschrift,' cxxxii, Orig.-Aufs., p. 1.

If these facts be given their due weight, it is easy to understand that a slight loss of alveoli may at one time produce a degree of respiratory disturbance greatly in excess of that which at another time attends a much more considerable loss. But it is evident in general that, *cæteris paribus*, the respiratory disturbance will be greater as the respiratory surface is diminished. The more extensive the infiltration, the compression, or the atelectasis, while the demand for oxygen continues as before, the less capable will the ordinary respirations be of satisfying this demand, and the more marked will be the dyspnœa. The mode in which the latter expresses itself under these circumstances is by no means always the same. As a general rule, it is true, the *frequency of the respirations* is increased. This applies, in the first place, to all those factors, of the category just discussed, which are accompanied by pyrexia, if for no other reason, because of the effect of the rise of temperature in accelerating respiration. It applies, next, to cases where a deep respiration would be attended by *pain*, and the breathing is therefore shallow, as in pneumonia and pleuritis; since in these cases the increase of frequency is the only possible means of augmenting respiration. Further, it is obviously true also, when large portions of the lungs are positively prevented from freely expanding, as in all somewhat considerable space-reducing factors in the thorax. And, lastly, in some cases it is the irritation of the terminations of the vagus in the lung, of which mention has been made in connection with bronchitis (vol. iii, p. 1006) that gives rise to an increased frequency of the respirations in a reflex manner. While we have here to deal with frequent and not abnormally deep, but as a rule shallow, respirations, both changes—*increased frequency and augmented energy*—may concur under certain circumstances, *e. g.* in the highest degrees of dyspnœa, such as arise in acute unilateral pneumothorax over a lung in which respiration was previously free, and more particularly in acute general pulmonary œdema. Yet the increase of respiratory frequency is very far from a necessary event in the category now under discussion; slow breathing is sometimes met with, *e. g.* in *emphysema* and in *open pneumothorax*, especially when this is bilateral. That it must be so appears from the Hering-Breuer law; for when, in extensive emphysema, the lungs cannot fully contract, expiration is not so promptly at an end, nor is inspiration so promptly called forth, as in a normal condition, and the breathing becomes retarded, there arises an *expiratory* dyspnœa. In pneumothorax an exactly opposite condition prevails, and the lung is unable to expand; and after making an incision through an intercostal space on both sides in the rabbit, you find that most *laborious and prolonged inspirations* are the result, while their number is very considerably diminished, but at once increases on occluding the openings.

That a bilateral open pneumothorax or a general pulmonary œdema, which does not rapidly pass off, must, despite the most vigorous dyspnœic respiration, very speedily terminate life, need hardly be mentioned: it is not so, however, with the other impediments to respiration of the last-described category. In these, dyspnœic breathing is a means of compensation of the most efficient and helpful kind. The extent to which, as a matter of fact, the organism is capable of meeting these obstacles by a change in the respiratory mechanism, we learn with numerical exactness from an interesting series of experiments by Weil and Thoma.* On injecting into one pleural cavity of a rabbit a moderate quantity of fluid cacao-butter, or on producing a closed unilateral pneumothorax by means of a fine trocar, they found that—just as in Köhler's animals with stenosis of the trachea—the *quantity of air respired in the unit of time* does not merely not decrease, but *increases*. This compensation has, it is true, its limits. When the quantity of cacao-butter injected is so great that the heart and mediastinum are pushed far over to the opposite side, and the diaphragm caused to arch towards the abdomen, or when one lung is rendered useless for respiration by making a widely gaping orifice through an intercostal space —in which case also there occurs a lateral displacement of the mediastinum and heart,—complete compensation is no longer possible; the animal then takes with each inspiration less air than in a normal condition, and since there is besides a fall in the number of respirations, the result must be a tolerably considerable reduction in the amount of air respired per minute. Moreover, K. Möller* found, in-patients suffering from lung disease, on determining by Pettenkofer's apparatus the excretion of carbonic acid, that their exchange of gases did not differ essentially from that of healthy individuals—a result fully borne out by daily experience in human pathology. It may happen now and then that a person quickly succumbs through asphyxia to a unilateral pneumothorax or to an infiltration or compression of the lung which extends rapidly; but that death does not necessarily occur is most strikingly taught by the far from rare instances of recovery from double pneumonia, from severe pleuritis with voluminous exudation, or even from unilateral pneumothorax. And though in many other cases where the impediment involves the alveoli, recovery cannot from the nature of the case take place, still it is within the daily experience of every physician, that in bilateral caseous infiltration, extensive cirrhotic condensation, large aneurysms, extreme emphysema, the patient's life may be greatly prolonged by means of the dyspnœic respiration.

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* Weil und Thoma, 'Virch. A.,' lxxv, p. 483.

As already pointed out, the permanent imperviousness of large groups of alveoli is not uncommonly attended by a *dilatation of the middle and smaller bronchi* leading to the groups as the result of the same inspiratory pull which brings about, in other portions of the lung, the compensatory inflation of the open alveoli. This happens chiefly in indurative and cirrhotic, so-called interstitial, processes in the lungs, and will the more certainly occur when at the same time firm adhesions, with a tendency to contraction, connect the two layers of the pleura, while the thorax is not so pliable or yielding as in a normal condition.

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* K. Möller, 'Ztsch. f. Biolog.,' xiv, p. 542.

Effects identical with or resembling those which impair respiration as the result of complete or partial stenoses of the air-passages cannot of course be expected to attend their *abnormal dilatation*, when the air may enter *in a manner different from* that which prevails in a physiological condition. For since the quantity entering the thorax is very far from increasing with the size of the opening—the amount being determined by the depth and number of the inspirations,—the respiratory exchange of gases is not at all influenced by enlargements of the lumen of the air-canal through defects due to ulceration, or, in the glottis, by muscular paralysis, or again by the presence of abnormal openings in addition to the natural orifice, as in wounds of the larynx and trachea. Not so, however, with *phonation*. For since this depends on the setting up by the expiratory stream of sonorous vibrations of the vocal cords, while these are approximated together and put more or less on the stretch, it will be rendered impossible, or at least impaired, if large portions of the cords are destroyed, or if, owing to paralysis of the recurrent laryngeal, they cannot be approximated, or if, lastly, the expired air finds a means of escape before reaching the glottis. Yet even if this function of our respiratory apparatus be altogether neglected, it is of great importance to respiration that *the air-passages form a comparatively long and narrow, closed and protected tube-system*. For, firstly, this is the most convenient and certain means of securing that the atmospheric air shall reach the pulmonary alveoli in a suitable condition, despite its enormous variations in temperature and moisture—although it appears that the supplying tube is unnecessarily long for this purpose. Experiments, which B. Heidenhain* carried out in my laboratory, have demonstrated that the length of the trachea alone is quite sufficient. When Heidenhain caused dogs to breathe air of different temperatures, either very much cooled or greatly heated, through a tracheal cannula, a thermometer pushed on as far as the bifurcation showed no noteworthy departure from the temperature of the animal's blood, provided the air inspired was *dry*. When, however, the hot air was saturated with vapour, the mercury rose rapidly, and there was accordingly developed in a short time an extensive croup of the trachea and bronchi, though the breathing of dry air was unattended by morbid consequences. The nature of this capacity of the organism to promptly equalise such variations of temperature has not been satisfactorily cleared up by Heidenhain; the importance of evaporation is clearly taught by the opposite results which attended the respiration of heated vapour, and it is not impossible, despite these striking contrasts, that had the inspiration of dry air been continued for a considerably longer period than the twenty to thirty minutes adopted by Heidenhain, there would then also have been a rise of temperature in the bronchi. There is another advantage, no less important and more easily understood, which accrues to respiration from the length and narrowness, the tortuous course of the air-passages, and the numerous folds and projections of their walls, namely, the protection of the deeper portions of the apparatus, and especially the respiratory surface, against the intrusion of bodies which should not enter them. For, normally, air, and *nothing but air*, should enter the lungs. A small amount of secretion must, it is true, be produced by the mucous membrane of the air-passages in order to protect them against drying, for the respiratory exchange of gases would be enormously impeded were the internal surface of the lungs covered by a kind of epidermis; still, as you know, the cilia by their movements secure that the mucous coating shall not normally be more than a very thin and delicate layer. If, however, any corpuscular particles are mingled with the inspired air, they become arrested at the bends and projections of the bronchi, and there remain till conveyed away, like the superfluous mucus, by the vibratory movements of the cilia.

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* B. Heidenhain, 'Virch. A.,' lxx, p. 441.

But, however admirably this protective mechanism may act, and though innumerable particles are arrested on their way to the alveoli and removed from the air-passages by the aid of the ciliated epithelium, yet the organism is very far from able to completely protect the lungs against the intrusion of foreign matters. This applies, in the first place, to the substances which are suspended in a state of minute divi-

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sion in the atmosphere. The air breathed by us is certainly *pure* above the snow-line on the sides of snow-covered mountains; but as for its claim to this title in inhabited and closely built districts, on this point the cities more especially have a story to tell. We need not go to factories and workshops, where clouds of the materials employed are constantly filling the atmosphere. Think of the masses of finely divided *carbon* or *soot* which fill the air of our busy cities and the rooms of the poorer classes, heated as they are by badly constructed stoves and lighted by inferior lamps. Think, too, of the dust of our roads and streets, which consists, as you know, of a mixture of *sand* and *chalk*, together with a great variety of organic particles. Now, of these impurities, a great portion will, it is true, be arrested in the larger air-passages; still a quantity will escape and pass through the entire bronchial tree till it reaches the alveoli, where it is no longer threatened by the ciliary movements. In addition to these minute particles, larger ones, to remove which the cilia are powerless, may, as I recently stated (vol. iii, p. 1007), occasionally gain an entrance to a perfectly healthy lung; and I then referred to the conditions under which this accident most readily takes place. Those who most frequently of all are exposed to it are persons who, for some reason or other, require to be fed artificially by the œsophageal tube; not because the tube may be falsely introduced into the trachea, but because during its withdrawal a few drops of the contents may only too easily be sucked into the larynx at the moment when the lower opening of the tube is passing the *aditus laryngis*.

But an event which, while the respiratory apparatus is intact, will happen only as a special accident, may, it is obvious, only too readily take place when the protective arrangements of the air-tube perform their functions imperfectly. These protective mechanisms consist, as you know, of the mucous membrane of the nose with the folds and elevations produced by the turbinated bones, of the epiglottis, and of the glottis, or rather the vocal cords. No one of these is useless, and there can be no doubt, for example, that more dust enters the lungs when the turbinated bones are destroyed and the exterior of the nose or its septum is defective. As a protection against coarser foreign bodies, however, the nasal cavity is of little moment, since the great majority of them enter the lungs from the mouth. In this case the epiglottis is certainly infinitely more important, although its value as a guard has often been exaggerated. During the normal act of deglutition the root of the tongue is so placed in front and above the entrance to the larynx that it suffices, without the aid of the epiglottis, to close the aperture against the ingesta. In dogs who had swallowed a strong dye made from alizarine, the epiglottis was found by Schiff* to have remained completely unstained; and how slight in reality is the protection afforded by the epiglottis against the entrance of foreign bodies is most clearly manifested by the fact that, after its extirpation in dogs, at most a few drops of liquid, but no solid masses or particles of food, entered the larynx during deglutition. With this fact our experience on man accords completely. Absolute paralysis of the depressors of the epiglottis—the thyro- and aryteno-epiglottidean muscles—has been observed in consequence of diphtheria of the pharynx and also in bulbar paralysis, in which cases the epiglottis stands up immoveable; and we have still more frequently the opportunity of seeing complete absence of the epiglottis as the result of syphilitic or tubercular ulceration: in such patients, however, there is no imminent danger that food or drink may escape into the air-passages—*so long at least as the glottis acts normally*. On the glottis rests the chief responsibility. The lungs of an individual in whom the vocal cords are intact, in whom the closers of the glottis can adequately contract, and in whom the mucous membrane of the glottis retains its sensibility, are not threatened to any extraordinary degree by foreign bodies. But the position of such a patient is proportionately serious when the vocal cords are more or less destroyed by ulceration, or when, owing to paralysis of the recurrent nerve, the mucous membrane has lost its sensibility and the glottis its power of movement. For the patient is then exposed not only to the danger that food may enter the respiratory apparatus during a meal, but to the risk that saliva and buccal mucus may at any moment flow into the trachea—just as in a rabbit after division of the vagi.

Lower than the glottis there is no special protective ratus within the air-passages, and when large particles have passed this point they cannot be arrested anywhere. Below it there is no necessity, it is true, for any special means of protection, because the rest of the air-passages form closed tubes which do not normally communicate either with the external surface of the body or with any of the internal cavities. Foreign bodies cannot, therefore, enter the air-passages below the glottis *except when the walls of the air-tube are somewhere interrupted.* By such an interruption, an open communication may be established between the larynx or trachea and the atmosphere, as occurs in tracheotomy, an operation so often performed at present that, in comparison, the extremely rare and very minute *congenital fistulæ of the trachea,* as well as carcinoma of the larynx perforating externally, are quite subordinate. Abnormal communications may also not uncommonly be produced between the trachea or a chief bronchus and the œsophagus, in consequence of epithelioma of the gullet; and such a perforating growth may often bring about a further communication with the pericardium, or with a gangrenous focus in the lung, or with the cellular tissue of the mediastinum. Moreover, a suppurating tracheal or bronchial lymphatic gland may not infrequently penetrate the air-passages, and I have already referred to the possibility that a large aneurism may open into the trachea or bronchus after gradually thinning their walls.

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* Schiff, 'Moleschott's Unters.,' ix, p. 321.

To all these must be added the various pathological products which, *originating in the respiratory apparatus itself,* are derived from the pulmonary tissue or bronchial walls, and have entered the air-passages. I refer, as you know, to the various catarrhal, serous, fibrinous, and purulent inflammatory products; further to blood, the transudation in mechanical hyperæmia, to shreds of necrotic tissue, &c.; and there is the less necessity to dwell on these processes as we have very recently considered them as factors by which the access of air to the bronchi or alveoli may be interfered with or prevented.

On that occasion we also thoroughly discussed some of the pernicious effects which arise for the organism from the presence of foreign substances in the interior of the air-passages, and you will presently hear of some other no less considerable evils. But if you reflect how numerous are the possibilities, and how great therefore the probabilities, that something besides air may enter the lungs, you will be inclined to wonder not so much that disturbances of the respiratory apparatus should rank so high amongst the diseases to which humanity is liable, as that there should be any individuals in existence whose lungs continue normal in constitution and regular in function. In fact, the respiratory apparatus of most of us would be in a much worse state than is actually the case, were it not that the organism has the power of *removing foreign bodies from the air-passages* in another way than by means of the ciliated epithelium. For this purpose it has recourse to the explosive expiratory impulses which we call *sneezing* and *coughing*. These are both *reflexly* initiated, as a rule, though coughing may also be voluntarily induced; and the two resemble each other in that *after a deep inspiration the air-passage is closed, and then suddenly opened by violent spasmodic, expiratory movements, accompanied by a loud noise.* In sneezing the closure is effected by the application of the soft palate against the wall of the pharynx, in coughing by the closed glottis.

The liability to sneezing displayed by different persons is very unequal. Many sneeze, you are aware, on simply looking at the sun; and indeed some people are attacked by it the moment the skin is exposed to a current of cold air. The situation, however, from which sneezing is by far most frequently initiated is the mucous membrane of the nose, or rather the sensory fibres of the trigeminus terminating in it. As for coughing, its true typical nerve is the superior laryngeal or its sensory terminations in the mucous membrane of the larynx. On touching the mucous membrane below the glottis, in a cat or dog, with a fine catheter introduced into the larynx, coughing is at once set up, especially, on the least touch, if the catheter comes into contact with the posterior wall. Yet it is not only the excitation of the nerves of the larynx that sets up coughing. In the trachea, the mucous membrane of the *pars fibrosa* is hardly less sensitive than that of the larynx, and in the remainder of the wall also the impulse to cough may be produced at least by forcible contact. It is very promptly set up by touching the *bifurcation*, and even when the catheter is pushed on into the bronchi, the animals cough, as a rule, as often as the mucous membrane is somewhat firmly touched.* But the coughing reflex may also sometimes be called into action from regions outside the respiratory apparatus, *e.g.* the meatus auditorius externus to which the auricular branch of the vagus is distributed, or the root of the tongue to which a small twig of the superior laryngeal passes ;† and particularly sensitive people cough even on exposure of the skin to a draught of cold air, *i.e.* on excitation from parts which are not supplied by the vagus. But in considering the subject one other point must be borne in mind, namely *that in a pathological condition there may be greatly increased sensibility to these reflexes.* This applies undoubtedly in a simple quantitative way to the usual seats of excitation. A person whose nose and larynx are healthy sneezes or coughs only when coarser particles or irritant gases enter the respective cavities. A person, on the contrary, with a cold in the head or a catarrh of the larynx, sneezes or coughs on breathing pure, cold, or very warm air, and more especially air containing dust; *i.e.* as the result of such trifling causes that the coughing is apparently *spontaneous.* This increased sensitiveness of the bronchial mucous membrane, this ready excitability of its sensory vagus terminations, explains why coughing occurs in bronchitis, not simply when the bronchi are filled by an abundance of muco-purulent secretion, but previous to this, before much secretion is produced, and especially too in *catarrhe sec,* of which the small amount of secretion is characteristic. No less dependent is the frequent coughing in all ulcerations of the mucous membrane of the respiratory apparatus, and chiefly of the larynx, on the increased irritability of the stumps of the sensory nerves, which have been deprived of their protective coverings by the ulceration. Furthermore, there is ample evidence to show that regions from which reflex coughing cannot normally be set up may become its starting-point in pathological conditions. This is probably the explanation of the fact that persons with fresh pleuritis generally feel a strong impulse to cough, although touching of the healthy pleura of a dog is not followed by coughing. Should it be thought, however, that because violent and persistent coughing sometimes terminates in vomiting, the cough is therefore reflexly excited from the stomach, this is, in my opinion, an erroneous idea. For to say nothing of the fact that in persons who vomit readily, and hence especially in children, the forced expiratory impulses accompanying coughing may give rise to vomiting directly by expressing the contents of the stomach, Edlefsen* has rightly called attention to the ease with which tenacious masses of secretion, when coughed out of the bronchi, may adhere to the posterior wall of the pharynx or to the velum, and from these sensitive spots may initiate vomiting. It has not hitherto been possible in physiological experiment to excite coughing from the stomach, and you will do well, I think, in meanwhile refusing to accept the occurrence in pathology also of a "stomach-cough."

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* Nothnagel, 'Virch. A.,' xliv, p. 95; Kohts, ibid., lx, p. 191; Störk, 'Wien. med. Wochenschrift,' 1876, No. 28, *et seq.*; Kandaraski, 'Pflüg. A.,' xxvi, p. 470.

† Brücke, 'Vorles. üb. Phys.,' ii, p. 97.

Yet we have to deal not only with a morbidly increased inclination to sneezing and coughing, but also with *a diminution of irritability of the mucous membrane in question.* That persons whose larynx is anæsthetic will not cough, even during an attack of laryngitis, and that comatose patients will not react by a fit of coughing to every fragment of food that may enter the larynx, I needly hardly say. But you all know from daily experience to what extent a habitual snuff-taker may succeed, despite the perfect sensibility of his nose, in dulling the nasal mucous membrane to intense irritants. The same effect is very commonly produced on the bronchi by persistent catarrh. Even in acute bronchitis the coughing is not of course continuous, because for its reflex initiation, not the minutest drop, but a certain quantity of secretion is required, and especially the contact with a highly sensitive spot in the bronchial tree. In chronic bronchial catarrh—that depending on bronchiectasis, for example—very large quantities of secretion must accumulate before coughing ensues, and in these cases consequently nothing is commoner than its occurrence in fits or regular paroxysms separated by considerable intervals.

By these reflexes of coughing and sneezing, the former of which is incomparably the more important in pathology, *all liquid or solid foreign matters which are present in the larynx or nose are propelled outwards*, and thus as far as possible removed from the respiratory canal. No such removal follows, it is true, when the reflex in question is set up without any foreign body in the air-passages, as in sneezing from exposure to a dazzling light or coughing through irritation proceeding from the meatus; as in purely nervous *hyperæsthesia* of the larynx, and especially too in the early stages of every rhinitis, laryngitis, or bronchitis, in which, while the mucous membrane is already abnormally irritable owing to the inflammatory hyperæmia and swelling, there is as yet no considerable secretion. Laryngeal catarrh, however, does not usually even in its subsequent stages give rise to much secretion, and I have already referred to the forms of bronchitis which are throughout almost free from it. Again, if the coughing depends upon the presence of ulcers with a scanty discharge, or of a small fixed tumour in the larynx, it usually continues dry; and just as we formerly became acquainted with infective diarrhœas (cf. vol. iii, p. 964), *i. e.* with diarrhœas which are conditioned, not by an enteritis, but simply by an augmentation of the peristaltic movements called forth directly by the virus, so I believe we must look upon *tussis convulsiva* as an *infective cough.* Not merely is it an old experience that in whooping-cough only small quantities of secretion are produced by the mucous membrane of the air-passages, but all unprejudiced observers are agreed that in this disease the inflammation of the larynx and bronchi bears no relation to the violence of the paroxysms of coughing. This being so, shall we really be over-venturesome in assuming that the virus of whooping-cough calls forth the paroxysms of coughing by direct and immediate irritation of the laryngeal or bronchial mucous membrane without the intervention of a laryngo-bronchitis? But, however this may be, since there is little secretion produced in whooping-cough by the mucous membrane of the air-passages, but little is expectorated during the height of the disease by the spasmodic paroxysms of coughing.

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* Edlefsen, 'D. A. f. klin. Med.,' xx, p. 200.

But if anything capable of removal be present in the re-s [illegible]nal, it is expelled by the expiratory impulses known as coughing and sneezing. The materials thus got rid of are very different in kind. In sneezing, it is usually either a foreign body, such as snuff, or a watery or mucous secretion. In coughing, foreign bodies also play a great part, and chief amongst them solid or liquid constituents of the food. The commonest form of accident is for a crumb or drop to enter the larynx, and then, on touching some part of the mucous membrane beneath the glottis, to set up a fit of coughing, which generally terminates with the expectoration of the crumb. It is not always possible, however, to remove the foreign body by the first few efforts. It may indeed be sucked deeper into the bronchi by the inspiration preceding the coughing, and, if angular or pointed, may there become firmly impacted, so that the most violent paroxysm fails to remove it; or the impulse may force it upwards, but fail to carry it through the glottis, so that it is drawn back into the lung by the next inspiration and may pass into another bronchus, perhaps of the opposite side. This may even be often repeated, and usually gives rise to very striking and characteristic symptoms, owing to the change in position of the bronchial occlusion. The second, and fortunately much less common, way in which pieces of food may enter the bronchi is through an abnormal communication between the œsophagus and the trachea. Here also the coughing follows quickly on the taking of solid or liquid food, though usually a little later than in the first mode, not so much because the portions of food now enter the air-passages from the lower section of the gullet as owing to the greater sensibility of the laryngeal mucous membrane.

But when emphasising the variety of the materials expectorated, I did not refer so much to the foreign bodies coughed up as to the different pathological products, which, whether originating in the respiratory apparatus or entering from without, are got rid of by coughing. From a theoretic standpoint—or if you prefer it, from the standpoint of general pathology—the variations do not appear to be great, for we have almost invariably to do with blood, the products of inflammation, or with portions of necrotic tissues. Consider, on the other hand, what enormous differences are met with, not merely in the amount of expectoration, but especially in the relative proportions of the constituents just mentioned; consider, further, how unlike are the products of the various forms of inflammation, and, lastly, what changes may be produced in the secretions and inflammatory products by secondary influences, *e. g.* putrefactive decomposition, and you will certainly find it intelligible that the subject of *expectoration* should have become a well worked-out and much studied chapter of special pathology.* For practical medicine, the importance of this chapter must be very highly rated, in particular because the examination of the expectoration forms in many cases an indispensable aid to the diagnosis of pulmonary diseases.

It is obviously beneficial to the organism that foreign bodies which have entered the air-passages from without should be expelled by coughing. Yet this also holds good essentially of the proper pathological products which are expectorated. For the ejected matters are, it is true, withdrawn from the body, and the expectoration consequently involves a certain loss of highly organised material. Still if you take the trouble to dry a quantity of sputum you will see at once how extremely slight the residue is—a portion of which, moreover, consists of ash-constituents. Consider in addition that the expectorated matters are in great part necrotic or in a state of putrefaction, that they are materials which had they remained in the organism might have proved injurious, but certainly could not have been of much service to it.

The act of coughing is not in itself an unimportant occurrence. A solitary cough has of course no significance whatever, and even an ordinary paroxysm due to the entrance of a piece of food into the larynx can scarcely prove injurious to a healthy individual. It is not so, however, when the cough is associated with a spasmodic forcible contraction of the glottis-closers, and consequently with a spasmodically intensified action of the expiratory muscles, more especially when this spasmodic coughing is frequently repeated, as in tussis convulsiva. It must not be forgotten, too, that those who cough much, and chiefly in violent paroxysms, are very far from healthy, and are in the great majority of instances patients whose respiratory apparatus does not perform its functions quite normally during the intervals between the paroxysms. That a violent paroxysm of coughing and spasmodic cough belong to the most painful and exhausting affections, everyone must be aware who has once witnessed such a paroxysm in a person with *catarrhe sec* or in a child with whooping-cough. But to pass over the suffering produced by the coughing, two apparatus are chiefly endangered by it, the circulatory and the respiratory. The paroxysm influences the circulation by causing a *rise of arterial pressure* through the very vigorous contractions of the expiratory muscles, but more especially by destroying the negative pressure in the thorax and even converting it into positive pressure, and thus *impeding the entrance of the blood from the systemic veins into the heart.* A glance at the enormously swollen jugular and facial veins, distended almost to bursting, and at the bluish-red hue of the face, teaches how important is this impediment during a paroxysm of coughing. Yet these phenomena speedily disappear when the attack is over, and even in long-persistent catarrh with very frequent and violent paroxysms the most that usually results is a certain varicose dilatation of the superficial veins. So much is this the case that when a patient who coughs gives actual evidence of a lasting increase of tension in the veins, it will be well for you to examine whether there is any other cause to account for it. It is less by chronic than by acute effects that the coughing threatens the circulatory apparatus; the chief danger arises from the sudden, very considerable rise of pressure undergone by the blood-stream in the smallest vessels. As you will remember, we referred on a former occasion (vol. i, p. 391) to paroxysms of coughing as one of the factors causing rupture of perfectly healthy capillaries. And though the bleedings thus conditioned are usually nothing more than harmless ecchymoses of the conjunctiva, &c., a paroxysm may prove actually fatal if the cohesion and resisting power of the vessel-walls have been much reduced by any kind of antecedent disease.

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* Vid. especially Biermer, 'D. Lehre vom Auswurf,' Würzburg, 1855, together with the newer text- and hand-books.

The prejudicial effects exerted by the paroxysms on the respiratory organs depend upon the circumstance that in coughing a very forcible expiration coincides with a closure of the glottis. This of course is ultimately overcome, but till then the air filling the lungs must be placed under very considerable tension. Yet the tension will *not*, you notice, *be everywhere equal*; for the contraction of the expiratory muscles, which reduces chiefly the lower aperture of the thorax and forces up the diaphragm, will most strongly compress the lower sections of the lungs, and as far as possible drive the air out of them. This air, however, will be driven with equal force into the upper sections, over which the thorax is but little narrowed even by forced expiration; and the result is, that owing to the pressure caused by the rush of air, the smaller bronchi become dilated and the alveoli torn, *i. e. bronchiectases* and more especially *emphysema* are developed. These are the forms of emphysema which occupy chiefly the upper portions of the lungs; and if emphysema of the upper lobes is occasionally found in persons who play wind instruments and in workmen who have to carry heavy loads or to undergo other violent exertion, I need scarcely say that the mechanism of its origin is precisely the same as in that which results from coughing. For the rest, it is not exactly a rare accident for the air, during a violent attack of coughing, to escape through the ruptured alveolar wall into the subpleural and interlobular tissue, so that the *vesicular* becomes complicated by an *interstitial emphysema*. And should there be present in the superior lobe, more especially in its anterior portion, a superficially situated cavity covered over by a thinned or partially necrosed pleura, the coughing, as was recently stated, may give rise to a sudden pneumothorax.

It is accordingly clear to you that a cough will often enough become the subject of the physician's treatment. More particularly when there is no proper object on which the cough can act, *i. e.* when there is nothing in the lungs to be removed by the expiratory impulses, it is unquestionably the duty of the physician to seek to modify the irritation by all available means. In cases, however, where the coughing is produced by the presence of foreign removable masses in the air-passages, such an attempt would have little to recommend it, were not an effort at the same time made to check the pathological processes to which the masses owe their origin. For the treatment might otherwise be productive rather of evil than good, by bringing about all the bad effects which ensue to the respiratory apparatus from the presence of foreign matters in the air-passages.

These bad effects are unfortunately only too frequently observable. For however excellently the mechanism of reflex coughing is adapted to the end in view, *it often fails to secure it.* For coughing to occur at all, it is indispensable that the mucous membrane of the air-passages should be sensitive, the glottis capable of closing, and the muscles of expiration so far functional as to be able to overcome by their contraction the closure of the glottis; for expectoration, still more energetic and effective contractions will be needed. Now I have already referred to the circumstances in which the reflex fails to act, owing to deficient sensibility of the respiratory mucous membrane; a comatose patient or a person with an anæsthetic larynx does not immediately cough, we said, if a morsel has entered the larynx—although such patients are specially exposed to this danger. Moreover, the reduced sensibility of the bronchial mucous membrane, to which reference has so often been made, may tell in a most undesirable way in persons with abnormal communications between the œsophagus and the air-passages—in persons, that is, who are absolutely unable to guard against the entrance of foreign substances into the bronchi, and who therefore, more than others, are compelled to rely on the promptness of the coughing reflex. Our experience with regard to the rima glottidis is very similar. I need hardly repeat that in individuals whose glottis stands wide open and immobile, or whose vocal cords and perhaps epiglottis are destroyed, all possible kinds of foreign bodies may very easily escape into the air-passages; and it is precisely these patients who, owing to their inability to close the air-passage, are no more able to cough properly than are individuals with tracheal fistulæ; which latter, again, give every facility for the access of foreign materials to the respiratory canal. In the last place, with regard to the third necessity, the functional capacity of the muscles of expiration, we are not rarely taught that the "adaptation" to its purpose of the reflex mechanism of coughing is perfect only in the case of healthy and vigorous organisms. None are more disposed, as is well known, to catarrh and accumulation of muco-purulent secretion in the bronchi than persons passing through a tedious fever, and precisely in these patients there is often developed early in the disease such a degree of muscular feebleness that vigorous coughing is quite beyond their power—even when the effort is not voluntarily suppressed, as in trichinosis, owing to the pain occasioned by it. Similarly, when in little children a foreign body enters the air-passages during play or at meals, coughing follows, it is true, but the expiratory impulses are far from being always powerful enough to expel the foreign body. And I need hardly say that the most energetic efforts of the expiratory muscles of a powerful man may occasionally fail when the foreign body has become impacted in a bronchus, or, if pointed, has partly penetrated its wall. As regards the question engaging our attention, however, the greatest importance attaches to the fact that *coughing cannot be initiated from the alveolar walls.* For it follows that any portion of a foreign substance which has completely passed the bronchi must remain henceforth in the lung, unmolested both by the ciliary movements and by coughing. The dimensions of these foreign bodies must of course be very minute; still it is precisely such bodies that most abound in the atmosphere as organic or inorganic dust; and even when coarser particles or liquids enter the bronchi, one must be prepared to expect that minute fragments or drops, which are not coughed up with the rest, may reach the alveoli and remain in them.

When a foreign substance has established itself in the air-passages, what follows will be determined by the nature of the substance, and especially by its chemical composition. It has repeatedly been found that larger foreign bodies, having a smooth surface, globular in form, and consisting of inorganic, non-decomposable material, may remain impacted in a bronchus for weeks or months without exerting any influence but the mechanical one, already discussed, of producing more or less complete occlusion of the bronchial tube. Still this is a rare occurrence, if for no other reason because the paroxysms of coughing generally sooner or later secure the expulsion of precisely such foreign bodies. Much greater interest is, therefore, excited, owing to their great commonness, by the fate and action of fine inorganic, and hence non-decomposable, foreign bodies, in a state of such minute division that they are not arrested in the bronchi, but penetrate into the alveoli. Nevertheless, it is only recently that this subject has been thoroughly studied. It was very early known that particles of dust reach the finest bronchi with the inspired air, and such particles were long ago observed in the interior of large epithelioid cells in the pulmonary alveoli, but without their being regarded as anything more than an interesting curiosity. Hardly more than ten years ago this important domain of pathology was first opened up by the observations of Traube* on *inhaled wood-carbon*, and above all by Zenker's excellent research on *dust-inhalation diseases of the lungs*. But even then there was an unwillingness, and almost a refusal, to draw the natural conclusions from the newly acquired results. And so, strange to say, the dispute has been active and long continued with regard to the substance chiefly involved in this question, namely *finely divided carbon*. And yet nothing is more certain than that *the whole of the black pigment of the lungs and bronchial glands*—the pigment usually briefly termed *pulmonary pigment* or *lung-black*—consists only and solely of *inspired carbon*. The soot suspended in the atmosphere is, it is true, in great part arrested by the nose and bronchi, and removed from the latter by the ciliated epithelium; but a not inconsiderable quantity penetrates as far as the alveoli, and *thence into the tissues and lymph-spaces of the lungs*. This the free granules can apparently accomplish independently; yet some are first taken up in the alveoli by roundish cells, of which it has not yet certainly been made out whether they are epithelial cells derived from the alveoli or altered colourless corpuscles, and are then by this means transported into the lymph-stream. The lymph-stream in fact receives all the particles of soot, which enter it chiefly from the borders of the alveoli toward the infundibula, and the ultimate situation of the carbonaceous material depends on the direction and anatomical arrangement of the lymph-channels. The particles very rapidly (within a few hours) reach the bronchial glands, where they first settle in the sinuses of the cortex and then in the follicles; not till much later do they penetrate the medullary trabeculæ. At the same time, however, the particles of soot are being distributed throughout the pulmonary tissue itself, and gradually accumulate in greater quantities where large masses of connective tissue are present, *i. e.* in *the adventitial sheaths of the vessels and bronchi*, in the coarser *septa* and the *subpleural tissue ;* though here too, it is true, they are never evenly scattered, but always collect into circumscribed spots or foci. The size and number, and therefore the closeness of the grouping, of these foci depend on the amount of inhaled carbon, hence mainly on the atmosphere of the place in which the person affected resides. But leaving these quantitative differences out of account, we always meet *post mortem*, even in children and people who have resided in the country, with the constantly recurring, typical picture, in which the pulmonary tissue as well as the pleura pulmonalis is studded and sprinkled over with black spots, and the bronchial glands are more or less *smoky grey* on section. These appearances are found in individuals whose respiratory organs have performed their functions excellently till death, in those who have perished as the result of an accident, of cholera, or of some other acute or chronic disease not involving the respiratory apparatus, and also in individuals who have succumbed to a pneumonia or other acute or chronic pulmonary affection, except that in the latter case the changes peculiar to the disease are also present. For the pure carbon is a *perfectly indifferent substance* to the lungs; hence, however great the quantity taken up or long the period of inhalation, the lungs continue to contain air in all their sections.

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* Traube, 'Ges. Abhandl.,' ii, pp. 511, 765.

It is rarely that carbon forms the sole impurity of the atmosphere, however ; and though many other minutely divided inorganic matters, such as potter's clay or powdered ultramarine, prove equally innocuous to the lungs, when suspended in equally fine particles in the atmosphere, there are unfortunately a large number of impurities which are far from being so indifferent. Here I include all inorganic bodies considerably larger than the carbonaceous particles, but not too large, of course, to enter the alveoli, such as coarse granules of sand and chalk ; angular or pointed substances, which may cause mechanical injury ; and the innumerable vegetable or animal particles which become mingled with the air of our streets in the form of *fibres of cellulose* or *horny fragments*, derived from our garments, from the skin of men and animals, and especially from *horse-dung;* owing to their lightness such particles may be swept into the air by every breeze. All of them when inspired can reach the pulmonary tissue and bronchial glands from the alveoli, just as do the particles of carbon; but *their action is different.* They have not the power of producing suppuration, like infective substances, and no abscess or ulceration develops around them; but neither are they quite innocuous. As in the case of every bland foreign body, there takes place in their vicinity a *slow, adhesive inflammation, which, by producing connective tissue, gives rise to the formation of a capsule;* according to the quantity and nature of the foreign material and the locality where it is lodged the resulting appearances will be very different. The origin of these inflammations in the inhalation of foreign bodies is most strikingly and clearly observable when the materials inhaled are distinguished by peculiar qualities as foreign to the organism. It was *siderosis pulmonum, i.e.* the *red* lungs of the mirror-polisher, who for months and years inhales the dust of the so-called *caput mortuum, i. e.* the powder of ferric oxide, which Zenker took as starting-point in his investigation.* Nor can the *stone-mason's lung* be mistaken by anyone who has once observed it; for the dirty grey nodules which are distributed throughout every part of the organ, which project beneath the pleura, surrounded as a rule by a ring of carbonaceous matter, and are scattered in large numbers through the bronchial glands, are so hard as to be easily distinguishable from miliary tubercles, to which in size and colour they bear an undoubted resemblance. On cutting through the stone-mason's lung, the knife grates upon the resisting tissues, and the surface of the section is rough, and feels like a grater to the finger. But the domain of these inhalation-processes is much more ample, and includes many forms of chronic pulmonary disease, in which the cause is not so obvious as in ultramarine-, ferric oxide-, and stone-mason's lung. I at least am convinced that the great majority of the cases described as *interstitial* and *cirrhotic indurations*, as *slaty induration*, and as *fibrous peribronchitis*, are nothing but the effects of *dust inhalation*. True, this view cannot be so certainly established here as in stone-mason's lung and siderosis, for it is almost never possible to detect the causative foreign body in the midst of the callosities and fibrous foci. But consider that many of the smaller foreign bodies have not such a characteristic structure or constitution that their demonstration would be easy and certain, and bear in mind, above all, that they are not permanent but may disappear, though only after a considerable time, through the metabolism of the organism. In an investigation carried out in Langhans' laboratory, v. Ins* discovered, besides many other valuable facts bearing on the process now engaging our attention, that *calcareous particles* may so completely disappear, in the course of a few weeks, from the lungs and bronchial glands, that no carbonate of lime can afterwards be detected in them. If then the calcareous granules are unable permanently to withstand the metabolism of the organism, the cellulose fibres, which I have just told you form a considerable portion of the dust of our streets, will certainly fare no better. But the new-formed callosities and masses of connective tissue do not disappear with the foreign bodies; their contraction at most continues, in consequence of which the alveoli are liable to perish, and, as already stated, bronchiectases are apt to be formed. That the indurations should tend to be slate-coloured, and the peribronchitic nodules should usually have a smoky-grey hue, while the bands of cirrhotic tissue are not uncommonly deep black, you will no doubt yourselves be able to explain, for all the chronic inflammatory products derive their colour simply from the soot inhaled previously, or at the same time with the exciter of inflammation. You observe what importance attaches to this group of inhalation-diseases in human pathology. For if the view just expounded be correct, a considerable proportion of the diseases usually embraced in the collective notion of *chronic pulmonary phthisis* really belongs to the class of inhalation-processes. The term phthisis is, in fact, perfectly applicable to them, if it be used to express simply that large sections of the lung have ceased to perform their function, and are "wasted;" but if the notion of phthisis be extended to the entire organism—a usage sanctioned by generations—the including of the inhalation-diseases with pulmonary consumption is calculated to lead to serious error. For the individuals affected with stone-mason's lung, siderosis, or anthracosis, though often exhibiting bronchial catarrh, do not as a rule suffer from fever; and so little are they disposed to general emaciation or hectic that they remind one rather of cases of emphysema or mitral insufficiency, in which, as is well known, the strength and nutrition continues good, so long at least as the compensation is adequate. How it happens that the human lungs should so very often be the arena of the inhalation-processes, while the lungs of animals are almost completely protected, is not difficult to comprehend. For to say nothing of wild animals which breathe the air of the forest, the atmosphere of the houses in which our domestic animals pass the greater part of their short existence, though not always agreeable, is constantly *moist* and therefore *free from dust*. Dogs, the constant companions of man, might, it is true, be endangered; yet in their case also there are many factors serving to protect them, *e. g.* their much shorter lives, and more especially the structure of the nasal cavity, which is much longer and better furnished with folds and recesses admirably adapted to catch the particles of dust; for the rest, the black lung-pigment is far from absent in such animals, and one frequently meets, in their subpleural and proper pulmonary tissues, a few hard nodules and fibrous patches, agreeing in every respect with the products of the human inflammations due to inhalation.

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* Zenker, 'D. A. f. klin. Med.,' ii, p. 116.

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* v. Ins, 'A. f. exper. Pathol.,' v, p. 169.

But all the bodies arriving in the lungs have not the same bland characters, and the resulting inflammations will not be so benign and productive. The classical example of these severer forms of inflammation due to foreign bodies is the so-called *vagus-pneumonia of the rabbit*. Rabbits cannot cough, any more than vomit, probably because their expiratory muscles are not sufficiently vigorous to bring about by their contraction, in opposition to the over-filled abdominal viscera, a considerable diminution of the thorax; if, consequently, the glottis-closers are paralysed and the rima stands immoveably open, these animals are greatly endangered by foreign bodies, which can only be removed from the air-passages by means of the ciliated epithelium. But the ciliated epithelium is not much of a safeguard, and fails completely when large quantities of food or buccal mucus enter the larynx; and you will not be surprised to hear that, after division of the recurrent laryngeals in the rabbit, there is always developed, during the few following weeks, bronchitis and an insidious and slow true *pneumonia,** which often spreads over large sections of the lungs. The infiltrated lobes are enlarged and heavy; on section they are firm, finely granular or smooth, yellowish or greyish white in colour, and thus remind one of caseous hepatisation in man. But although this resemblance is apparently supported by the presence in the infiltrated alveoli of considerable quantities of large epithelioid cells, to which Buhl attached such importance that he invented the unfortunate name of "desquamative pneumonia" for the affection, yet the entire process has nothing whatever in common with human phthisis, the specific caseous or tuberculous pneumonia. For it cannot be communicated by inoculation to other rabbits or guinea-pigs, nor do the animals with divided recurrent nerves ever develop tubercles or tubercular formations elsewhere; the process is nothing but a common pneumonia, with a slow and chronic course, in which, owing to its protraction, time is allowed the exudation-corpuscles to develop and become converted into large cells. This pneumonia following division of the recurrent laryngeals is distinguished from the pulmonary inflammation by which the animals are attacked after section of the vagi in the neck† solely by its prolonged course. Should any one suppose, however, that this striking disparity in time, renders it unlikely that the paralysis of the glottis—which must occur equally after section of the vagi or of the recurrent nerves—is the main factor in the pulmonary affection, I desire to remind him that after division of the vagi, not only are the glottis-closers but the musculature of the œsophagus paralysed, and the rabbit's mode of inspiration changed completely. The extremely deep inspirations now made by the animal actually *suck in the food-pulp*, which cannot enter the gullet already filled with food, *through the gaping rima into the lungs*; and thus after division of the vagi the foreign-body-pneumonia terminates the rabbit's life within the first twenty-four to forty-eight hours, while the animals may survive the section of the recurrent laryngeals for weeks or even months.

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* Cf. Friedländer, 'Virch. A.,' lxviii, p. 325.

† Cf. Traube, 'Ges. Abhandl.,' i, p. 1, 113; Genzmer, 'Pflüg. A.,' viii, p. 101; Friedländer, l. c.; O. Frey, 'D. pathol. Lungenveränderungen nach Lähmung d. N. vagi,' Leipsig, 1877; Steiner, 'A. f. Anat. u. Physiol.,' Physiol. Abth., 1878, p. 218. Cf. also Zander, 'Pflüg. A.,' xix, p. 263, who studied the consequences of bilateral division of the vagus in birds.

In man, also, severe *pneumonia, due to foreign bodies*, and terminating in suppuration or even in gangrene, is not uncommon. It sometimes happens that large objects, which have become impacted in the bronchi, though comparatively harmless in chemical constitution, prove dangerous by their mechanical effects. Jagged or very angular bodies, but also coins and rings, may produce by their continuous pressure necrosis and perforation of the bronchial wall, and while this usually terminates the stenosis, an inflammation ending in abscess is only too easily excited by the foreign body enveloped, as it is, in stagnant bronchial secretion. I recently had an opportunity of making a post-mortem examination of a child, aged four months, with double harelip and cleft palate, in whom, about fourteen days before death, a piece of the very prominent vomer was excised preparatory to the projected plastic operation. The child had on the left side a pyo-pneumothorax caused by the rupture of a pulmonary abscess, which itself was discovered to have originated from the irritation of a little fragment of bone of jagged shape and rough surface; this was impacted in a bronchus of the superior lobe, and had produced several perforations of the wall; it was a piece of the vomer from the vicinity of the defect left by the operation, the borders of which had undergone necrosis. Possibly, therefore, in this case, it was less the jagged shape of the foreign body than its origin in a carious-necrotic focus that gave rise to the formation of abscess. For the vast majority of all the foreign bodies that have to be considered in this connection are organic objects, which readily decompose, and have entered the lungs when decomposition had already begun—like some articles of food or particles from a cancer of the œsophagus—or have *rapidly fallen a prey to the action of bacteria almost always present in the inspired air.* The latter observation applies more particularly to fragments of food which have "gone the wrong way," or have entered the air-passages through an abnormal communication with the œsophagus, and for some cause are not expelled by coughing. Owing to the decompositions undergone by the foreign bodies, which are generally putrefactive in character, severe inflammation is set up around them; this, while lobular in form, is always extremely dangerous to life, because it leads to abscess or gangrene. As a matter of fact, a very considerable number of lunatics who are fed by force, of unconscious fever patients to whom nourishment is given by the nurse, of persons whose aditus laryngis cannot for any reason be closed towards the pharynx, and of individuals with cancer of the œsophagus, &c., perish in consequence of such gangrenous lobular pneumonia.

This brings us at once to the consideration of a variety of corpuscular impurity which is always present in all parts of the inhabited world, namely *lowly organisms.* That bacteria or their germs are suspended everywhere and at all times, in more or less large quantity, in the air surrounding us, need hardly nowadays be proved. This, however, implies that we are constantly by our inspirations introducing unnumbered quantities of bacteria into our lungs, and if, in spite of them, the organism lives on undisturbed and undamaged, I need hardly say that this result is due to its capacity of getting rid of the schizomycetes, or at any rate of rendering them innocuous. There is no doubt that numbers of bacteria are arrested by the mucous membrane of the air-passages and expelled by means of the ciliated epithelium; but it is no less certain that numerous examples of these organisms enter the alveoli, and, like the particles of carbon, pass on into the lymph-channels of the lungs, *i. e.* into the juices of the body. Whether they are destroyed in the lungs or bronchial glands, or in what other organs, is not known; but it is certain that *they are got rid of or destroyed,* for in a normal condition we do not find schizomycetes in the fluids and tissues of the body (cf. vol. i, p. 205). True, the inhalation of bacterial germs does not always prove such a harmless occurrence, and we must be prepared to deal with this factor, especially when there is present in the air-passages abnormal material which may form a good substratum for the settlement of the schizomycetes. Thus, if the stagnant secretion of a chronic bronchial catarrh undergoes putrid decomposition and a *putrid* bronchitis develops out of a simple one, this is most certainly attributable to the influence of inhaled bacteria. To the pernicious action of the schizomycetes on organic foreign bodies contained in the air-passages, we have just referred. Not only the fate of foreign bodies, however, but that of many foci of disease and morbid products, with which the inspired air comes into contact, is determined in an eventful manner by the bacterial germs contained in the air. They alone are the cause of the development of a *dissecting suppuration* around a hæmorrhagic infarct of the lung, a process which is extremely rare in the perfectly analogous infarcts of the spleen and kidney. Above all they are responsible for the fact that almost every necrotic focus of the lung, however conditioned, becomes the seat of a true *gangræna humida*.

Whether we have to deal in all these cases with identical, or at least allied, organisms, related to the true bacteria of putrefaction, has not been made out, but is scarcely probable. At any rate, Leyden and Jaffé* have found in the expectoration of putrid bronchitis forms of bacteria differing from the micrococci and from bacterium termo, and the *ferment* recently found by Filehne† in foci of pulmonary gangrene, but not present in putrefied pieces of lung, plainly tells in favour of the view that particular species of schizomycetes are here engaged. This question is chiefly interesting, however, with reference to some specific morbid processes, among which *tuberculosis* stands first.

The question is—Is the cause of *true tuberculosis of the lungs* and of specific *pulmonary phthisis* to be sought in substances arriving in the bronchi and alveoli with the inspired air and passing thence into the tissues of these organs? This substance is not, of course, blood. We, who have placed tubercle among the infective tumours and thereby declared that it is due to a specific virus, may dispense with special proofs that blood poured out into the bronchi and passing into the alveoli must be absolutely innocent of causing the disease. That many persons who afterwards become phthisical are attacked by hæmoptysis at a time when the most careful physical examination fails to detect disease of the lung is disputed by no one ; but therefore to infer that the pulmonary hæmorrhage has been the occasion of the development of phthisis could only occur to a person to whom the domain of experimental pathology had remained completely closed. For the first rabbit into whose trachea he had injected, or allowed to run from a divided artery, a quantity of blood, would have taught him that the blood is first *aspirated into the alveoli* by the dyspnœic inspiration which immediately set in, and is very soon transported, like the particles of carbon, into the lymph-channels of the lungs and the bronchial glands.* For these parts, however, the blood-corpuscles and still more the plasma are the most indifferent substances imaginable ; they rapidly disappear, without, as a rule, leaving a trace even of pigment. At present, when Robert Koch† has just astonished the scientific world by the announcement that he has succeeded in discovering the much sought-for virus of tuberculosis, and that it is a *bacillus*, which is constantly present in tuberculous products, and is well characterised by its morphological structure and behaviour towards stains,—at present, I say, we no longer have to discuss whether tuberculosis is caused by a *specific, corpuscular virus*, and need only ask whether this virus enters the body with the inspired air, or is taken up in some other way, perhaps by a wound or by the intestine. That either alternative is possible cannot of course be disputed *a priori*. But in estimating the probabilities in favour of one or other mode of infection, we cannot, in my opinion, evade the force of the rule, confirmed by the experience of all observers in every country, that *no organ is attacked with the same frequency or intensity by tuberculosis as the lungs*. It is extremely common to find that the lungs, with the bronchial glands and pleuræ, are the only localities affected by the tuberculosis ; and in many other instances both the clinical history and the post-mortem appearances teach that the disease of the lungs has preceded that of all the other organs. In this connection, note carefully how impossible it is that the respiratory apparatus should form a specially favorable seat for the establishment and development of the tuberculous process; for inoculation tuberculosis as well as the experiences of the sick-bed and post-mortem room show unmistakably that no organ possesses an immunity from tuberculosis, not only so but that all organs of the body—intestinal canal, kidneys, genitals, liver, spleen, bone-marrow, central nervous system, &c.—are nearly equally susceptible to tuberculosis. But if, despite this equal susceptibility, the respiratory organs are so decidedly preferred, does not this point indisputably to the conclusion that the lungs are the first parts met by the virus, or, in other words, that *they form the usual gate of entrance for the virus of tubercle?* In this view I am further specially strengthened by the circumstance that the bronchial and tracheal lymphatic glands are so very frequently and early attacked by the disease; thus it is nothing uncommon to meet an advanced and wide-spread caseation of these glands, while the process in the lungs is limited to the eruption of a few nodules, or to a slight caseous infiltration. This fact will at once remind you how certainly, and especially how rapidly, the inhaled particles of carbon find their way to the bronchial glands, and you will now recognise the justice of the assumption just explained, that the tubercular virus is, as a rule, taken into the human organism by the lungs. Let it be clearly understood, not in this way only; there is no doubt that the intestinal canal may also admit it, and the investigation of individual cases would probably reveal other channels of infection.* In the great majority of cases, I believe, however, that it may be unconditionally asserted that the tubercular virus enters the body through the respiratory apparatus, *that it is inhaled.* But if this view be correct, it follows that not only the indurative and peribronchitic processes formerly discussed, but the true indubitable pulmonary tuberculosis is at least very often an inhalation disease. From former lectures (vol. ii, p. 729, *et seq.*) you know why I—even before the new evidence was brought forward by Koch—was unable to admit a fundamental distinction between tuberculosis and scrofula, between the tuberculous formation of nodules and the caseous infiltration; and I need not explain that I include under true pulmonary tuberculosis, tubercle of the air-passages, parenchyma, and pleuræ, as well as caseous hepatisation and the caseation of lymphatic glands. I also include, of course, all the consecutive conditions arising therefrom, in particular the tubercular ulcers of the larynx, trachea, and bronchi, as well as the cavities formed in the lungs,—that disease consequently which usually gives evidence very early of its general character by the accompanying fever, and for which, owing to the almost constant appearance of general emaciation and feebleness, the expression "phthisis" is only too appropriate. This true phthisis is, I think, generally an inhalation disease; but it is due to the inspiration, not of any chance atmospheric dust, but exclusively of a definite *corpuscular, specific virus*, the *bacillus tuberculosis*. As regards the biology of this bacillus, Koch's investigations have already made us acquainted with some valuable facts; amongst others, that it reaches the atmosphere chiefly from the sputa expectorated by the phthisical. For the sputa more especially which are derived from phthisical cavities are often extremely rich in bacilli, and since these can in a dry condition retain their vitality and virulency for weeks, it is not surprising that the atmospheric air should only too frequently contain active bacilli. Indeed, if you consider how extremely common tuberculosis is, you will at once be convinced that the tubercular virus must be *extraordinarily widely disseminated*, at least in the regions inhabited by Europeans. Perhaps it is not much less widely distributed than are the various other constituents of dust, with which it is usually inhaled. Their occurrence in association and simultaneous inspiration, is the reason why phthisical lungs are so seldom seen without the presence also of anthracosis or of indurative and peribronchitic processes. And though, on the other hand, it is not everyone, fortunately, with induration of the apex or interstitial and cirrhotic thickenings of the lungs that develops phthisis, yet you will not forget that the mechanical or chemical effects of foreign bodies entering the lungs must follow inevitably, while an organised virus is not capable of flourishing and developing in every organism.

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* Leyden und Jaffé, 'D. A. f. klin. Med.,' ii, p. 488.

† Filehne, 'Erlang. physik.-med. Societätsber., Jun. 11, 77, Dec. 10, 77.

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* Nothnagel, 'Virch. A.,' lxxi, p. 414.

† R. Koch, 'Berl. klin. Wochenschr.,' 1882, No. 15.

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* Cohnheim, 'D. Tuberculose v. Standpunkte d. Infectionslehre,' 2 Aufl Leipsig, 1881.

But is tuberculosis the only infective disease, the virus of which enters the human organism together with the inspired air? I think not. One is most inclined to accept this mode of infection in those diseases whose chief situation is the respiratory organs themselves. That *influenza* and *whooping-cough* are infective diseases is questioned by no one; but who would venture now to decide whether many cases of ordinary *laryngitis* and *bronchitis* are not infective in character? I remind you, too, of *diphtheria of the larynx and bronchi*, of *pleuro-pneumonia* in cattle, and typical *croupous pneumonia*. In fact, it appears to me that anyone who is convinced of the parasitic nature of the different species of virus must find the assumption extremely seductive, that the virus of those infective diseases which are localised in the lungs is *inhaled*. Yet there exists, in my opinion, no fundamental reason for confining this assumption to the diseases localised in the respiratory organs. Now that all doubt has long ceased as to whether corpuscular matters may pass from the alveoli into the lymph-channels of the lungs, and thus arrive in the juices of the body, it is very conceivable that the virus of the malarial diseases, of relapsing fever, of typhus, &c., may be taken up in this way by the organism. The hypothesis appears to me to be at least worth discussing, and, so far as I see, is no less justifiable than the assumption of an infection from the intestine or even from a wound of the skin.*

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* In connection with this chapter, cf. the text-books of Canstatt, Wunderlich, Niemeyer, Lebert, the appropriate sections in v. Ziemssen's 'Handbuch, and especially the excellent exposition by Biermer in 'Virchow's Handb.,' v, 1, which, unfortunately, remained uncompleted.

CHAPTER II.

THE RESPIRATORY MOVEMENTS AND THE PULMONARY CIRCULATION.

Abnormal character of respiratory movements.—Their secondary and primary dyspnœic augmentation.—Their dimensions inadequate.—Impediments to inspiration.—Defects of the diaphragm.—Loss of contractile substance by the muscles of inspiration.—Paralysis of their nerves.—Abnormal resistances on the part of the abdomen and thorax.—Pain.—Impediments to expiration.—Tonic spasm of the diaphragm.—Rigidity of the thorax.—Deficient elasticity of the lungs.—Consequences to the interchange of gases.—Changes in the mechanism of respiration.

Abnormalities in the pulmonary circulation.—Exclusion and occlusion of blood-vessels.—Cardiac lesions.—Obstacles to change of volume of the lungs.—Regulation by means of hypertrophy of the right heart.—Disturbances and cessation of this regulation.—Dyspnœa.—The dyspnœic movements of respiration as regulators of the pulmonary circulation.

Influence of an abnormal constitution of the blood on respiration.—Cholera and anæmia.

WHILE discussing the disturbances of respiration arising from a faulty condition of the air-passages, it was implicitly assumed that *the apparatus carrying out the respiratory movements worked regularly, and that the circulation was perfectly normal;* for on these chiefly depends the possibility of that prompt regulation, by an alteration and strengthening of the mode of respiration, on which stress has so often and so emphatically been laid. Now this assumption is far from being always realised; you know what an important *rôle* is played in pathology by disturbances of the circulation, whether of the flow or constitution of the blood; and an abnormal behaviour of the apparatus carrying out the respiratory movements is so frequently observed by the physician, that anyone desiring to study the pathology of respiration can certainly not afford to leave these factors out of sight. For, to take the second, the respiratory movements, first; it is quite correct that these, even when most vigorous and regular, are worthless if air is prevented from entering the lungs, or if the lungs are kept from following the movements of the thorax; but it is no less true that even with the greatest degree of perviousness of all the air-passages and absolute integrity of the pleural cavities, an exchange of gases between the blood and atmosphere, sufficient to maintain life even for a short time, would be impossible if the movements of respiration did not constantly convey fresh air to the alveoli. The more fundamental, therefore, the importance of the movements to the process of respiration, the greater, naturally, will be the interest claimed by pathological derangements and abnormalities of these movements.

But what is meant by *faulty* or *pathological* respiratory movements? A new-born child breathes much oftener than an adult; the mode of respiration in a woman differs from that in a man; still greater differences are observable, however, in the mode of respiration of one and the same perfectly healthy individual within very short intervals. If you see a person who has just run rapidly up several steps breathing laboriously and frequently, perhaps panting for breath, will you therefore at once put him down as suffering from disease of the lungs? Certainly not, if after a short rest, you again observe the eighteen regular and easy respirations which a person of that age is accustomed to take per minute with the body at rest. No; such alterations in the mode of respiration, though sharp and extremely conspicuous, not only lie within the limits of health, but are even the direct expression of the physiological reaction of the organism to the change in the gaseous contents of the blood. That human life may be sustained and its functions progress regularly, it is indispensable that the oxygen contained in the blood should not fall below, and the carbonic acid should not rise above, certain limits, and to secure this is the office of the respiratory process. This it must do not only when the body is at rest, and under the ordinary average conditions, which may be termed the normal, but under all circumstances, however greatly they may deviate from the normal. To satisfy these varying demands the organism has recourse to changes in the movements of respiration. While the quiet, easy respirations ordinarily suffice, the movements are increased, in depth or frequency or both, so soon as for any reason the carbonic acid of the blood becomes abnormally excessive or the oxygen-contents fall below normal, and this continues till the normal standard is restored. Thus the laboured, dyspnœic breathing is the means of compensating for the increased production of carbonic acid during muscular exertion, and we have seen that the same regulative measure is employed in stenosis of the air-passages. When discussing the latter, I was able to show by figures how perfect is the regulation effected by the dyspnœic breathing; but that this is also the best means of correcting an excess of carbonic acid due to other causes, follows directly from the fact that the amount of this gas contained in the expired air undergoes an absolute increase either when the single respirations are deeper or their frequency greater than normal.

If the dyspnœic respiratory movements, occurring in stenosis of the air-passages, or the like, be regarded as pathological because they are due to a morbid condition, no exception can be taken to such a course; yet they must not, it is evident, be reckoned among the factors by which the respiratory process is impaired or deranged. But if this *secondary* dyspnœa cannot now be the subject of discussion, this is true no less of the vigorous movements of respiration which, in contrast to the former, may be termed *primary*. I refer among other things to the fact that a person can to a certain extent voluntarily alter his mode of breathing, and may, if he will, breathe more deeply or more frequently. As the result of certain emotional conditions, also, the breathing may be accelerated or deepened. Then, we meet, more especially in the hysterical, with paroxysms of short or longer duration, in which the respirations are extremely frequent and all the respiratory muscles engaged, so that the breathing actually resembles that of a hunted, panting dog. Another variety of primary augmentation of the movements of respiration, not depending on obstacles to breathing, is *heat-dyspnœa*, which always develops when the medulla oblongata is bathed by blood of abnormally high temperature. Yet, however striking these forms of dyspnœa may be, they have no importance whatever for the pathology of respiration. The fact that their duration is always brief is enough to render them insignificant. No one can long continue voluntarily to take forced respirations; the dyspnœic paroxyms of the hysterical never last long; and even towards high temperatures the energy of the respiratory centre is speedily exhausted. But their unimportance as regards the question engaging our attention is proved chiefly by the fact, established by the researches of Voit,* Pflüger,† and their pupils, that such alterations of the mechanism of respiration exert no influence on the gases of the blood except that involved in the increased work of the respiratory muscles. For it follows directly therefrom *that an increase of the work done by these muscles in excess of the existing demand of the organism for air is of no consequence to the respiratory process itself.*

It is not so in the opposite condition, *i. e.* when *the respiratory movements are inadequate.* You will willingly dispense with a detailed description of the normal process of respiration. For it is well known to you that the inspiratory dilatation of the thorax takes place through the contraction of certain muscles, in the male chiefly of the diaphragm and also of the external intercostals; while in the costal type of respiration in the female, in addition to the diaphragm the chief part of the work is done by the external intercostals, scaleni, and levatores costarum. The contraction of these muscles overcomes the resistance of the ribs and of the elasticity of the lung as well as that of the intestines and abdominal muscles, and in this way enlarges the thorax in its vertical, transverse, and antero-posterior diameters. On the other hand, you will bear in mind that ordinary quiet expiration is a passive process, and occurs, after the contracted muscles have relaxed, simply through the return of the parts, by virtue of their elasticity and weight, to the position occupied by them before their equilibrium was disturbed by the inspiration. Hence it evidently follows that the regular progress of *inspiration* depends above all on *the ability of the proper muscles to contract properly,* while normal expiration requires the *occurrence of muscular relaxation at the proper moment,* when *the elasticity of the lungs and ribs* effect the rest. Let us now see whether conditions are met with in pathology, in which one or other of these requisites fails to be met.

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* Voit, 'Zeitschr. f. Biol.,' xiv, p. 94, contains a *resumé* of his own and his pupils' researches.

† Pflüger, his 'Archiv,' xiv, p. 1.

In order that the inspiratory muscles may contract properly they must not only be *present,* but *normal in structure.* Imperfect formation of one of the respiratory muscles may sometimes occur on the wall of the thorax, but only when involving the diaphragm is it at all important. Here too, however, the evil attending small *defects,* whether congenital or the result of injury, does not consist so much in an interference with muscular contraction as in the danger lest some of the contents of the abdomen, *e. g.* the stomach or a loop of intestine, may escape into the cavity of the thorax. For it is precisely during and owing to the contraction that small apertures and rents of the diaphragm are closed, and the defect must consequently be large to directly damage inspiration. Unilateral complete rupture and total absence of one half of the diaphragm have, however, been observed, or *the organ may be altogether absent.* Yet even if the diaphragm and the other respiratory muscles are regularly formed and free from injury, their functional power may be considerably impaired by several factors. This will be the case more especially as the result of processes attended by a serious *loss of contractile substance.* The contractions can obviously only be feeble when the energy of the muscles has been greatly reduced by severe pyrexial disease, especially by typhoid; or when the diaphragm has undergone a fatty change—to the frequent occurrence of which in emphysema, bronchitis, and heart-disease, attention has recently been directed by Zahn;* or, still more, when the inspiratory muscles are extremely wasted as the result of great debility or in the course of progressive muscular atrophy. But a loss by displacement and destruction of large portions of muscular tissue, both in the diaphragm and the intercostals, &c., may also be brought about by dense and extensive cancerous infiltration, and the function of these muscles must no less suffer in consequence of inflammation, such as pleuritis and peritonitis diaphragmatica, in which a slighter degree of inflammatory œdema makes its appearance, or as the result of the more intense and severe effects attending an extensive *invasion by trichinæ*. The action of the inspiratory muscles will be still more interfered with, I need hardly say, by *paralysis* of the nerves supplying them. Such paralysis is, it is true, uncommon, but it may be due either to a central cause, *e. g.* injury or a focal disease of the medulla oblongata, or to a peripheral one, *e. g.* compression of the phrenic in the neck. Paralysis of the diaphragm has also been observed after lead-poisoning and in hysterical patients, and rheumatic paralysis of the diaphragm, intercostals, and scaleni has been described by neuro-pathologists. But even when the muscles and nerves are quite normal, the occurrence of an adequate contraction may be rendered impossible by an unnatural increase of the resistances to be overcome by the respiratory muscles. Here we are chiefly concerned with the abdomen, whose contents are compressed, and whose muscular wall is put on the stretch and protruded forwards by the inspiratory flattening of the diaphragm. The movements of the latter may be reduced to a minimum in a dog, or still better in a rabbit, by tightly applying an elastic bandage to the lower section of the thorax and the abdomen. This factor tells in pathology in another but no less effective way. When a large solid tumour, a great accumulation of fat, or a voluminous collection of liquid is present in the abdominal cavity, or when—the most frequent of these disturbances—the intestines are distended with gas so as to produce marked meteorism and to cause extreme arching of the diaphragm, this muscle is quite incapable of compressing the contents of the abdomen. Moreover, extensive ossification of the costal cartilages and the resulting rigidity and comparative immobility of the thorax, such as commonly accompanies pulmonary emphysema, must essentially impede the action of the levatores costarum. On the other hand, it is not easily conceivable that the resistances on the part of the lungs should ever grow so considerable as to be incapable of being overcome by the contraction of the inspiratory muscles. Have we not seen that when, for any reason, large portions of a lung cannot be expanded, the inspiratory pull produces an abnormal ectasis of the remaining distensible section, and thus gives rise to vicarious emphysema? Moreover, in the many cases where imperviousness of the minute air-passages, a condensation of the pulmonary parenchyma, opposes an abnormal resistance to the contraction of the inspiratory muscles—in extensive pleuro-pneumonia, for example—a circumstance of a very different kind contributes to lessen the activity of these muscles, namely, the *pain*. The patient instinctively avoids everything that might aggravate the stitch and discomfort, and he, therefore, early in the disease commences breathing as superficially as possible, so as to guard to the utmost against stretching and movement of the inflamed pleura. That the pain is also an additional factor, enfeebling the inspirations of persons suffering from trichinosis, you will be the more ready to credit on remembering that the trichinæ are inclined to invade by preference the diaphragm and intercostals. Recent fractures of the ribs will act in the same direction; in short, any pain setting in at the height of inspiration, whatever its cause, may render the breathing shallow, as was long ago pointed out by Traube* with regard to perityphlitis.

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* Zahn, 'Virch. A.,' lxxiii, p. 166.

The factors that are calculated to interfere with expiration are of a different character. As regards the action of the muscles, in the first place, the effect produced by paralysis of the diaphragm on inspiration is analogous to that resulting from *tonic contraction* of the same muscle to expiration. For it is obvious that so long as the diaphragm continues tonically contracted, *i. e.* in the position of deep inspiration, the lungs cannot diminish. Since, however, the relaxation of the contracted inspiratory muscles is only a necessary preliminary to the expiratory diminution of the thorax, which is brought about by the weight and elasticity of the thorax and lungs, the regular relaxation of the diaphragm does not guarantee a normal expiration. Rather, the rigidity and immobility of the chest-wall, to which reference has already been made, must prove prejudicial to expiration; and, above all, we cannot count upon the prompt and sufficient diminution of the thorax if the lungs do not retract energetically. We have already (vol. iii, p. 1025) discussed the circumstances under which the elasticity of the pulmonary tissue is diminished, and we then dwelt on the fact that this occurs in a very eminent degree in *volumen pulmonum auctum* and in *true emphysema of the lungs*. The spontaneous contraction of the thorax is most difficult when the emphysema involves both lungs, and the greater part of their tissue is converted into a system of more or less large, very thin-walled, lax and inelastic air-sacs; and certainly the importance of such conditions is in this respect much greater than is that of much larger phthisical or bronchiectatic cavities, when these are confined, as is usual, to the superior portions of the lungs.

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* Traube, 'Ges. Abhandl.,' ii, p. 53.

But whether inspiration or expiration is interfered with, the immediate result, so far as the gaseous contents of the blood are concerned, will be the same. For if, from any cause, the thorax is less dilated during inspiration than it normally should be, the normal amount of air, rich in oxygen, cannot penetrate to the alveoli; and if, on the other hand, the thorax and lungs are unable to contract in regular fashion during expiration, the air of the alveoli, containing carbonic acid, cannot escape as it should do. The result is the remaining over of too large a quantity of residual air, which, itself useless, prevents the fresh air from reaching the respiratory surface. The condition, you perceive, exactly resembles that in stenosis of the air-passages. And just as in the latter, the reduction of the respiratory exchange of gases would here also, according to its degree, sooner or later terminate life, had not the organism at command two excellent means of regulation, of which it makes use in stenosis, namely, reduction of oxygen-consumption, on the one hand, and modification of the respiratory movements, on the other. You will not require me to go into the first mode, and to explain that the patients are able to limit the production of carbonic acid chiefly by reducing as far as possible their muscular work; but a short discussion of the second point may be more desirable, as in these cases the control of the organism over the respiratory muscles is not without its limits.

Too feeble and inadequate inspiration is compensated either by *transferring the work from the incapable muscles to other more capable ones, or by increasing the frequency of respiration.* When the descent of the diaphragm is prevented by the presence of a large tumour or collection of fluid in the abdomen, or when this muscle is degenerated, atrophied, or paralysed, respiration in the male also assumes the *costal* type; *i.e.* the contraction of the intercostals and scaleni brings about the dilatation of the thorax quite sufficiently when the body is at rest, while in laboured breathing the levatores costarum, serrati, &c., are called upon for aid. It is thus possible to maintain respiration even in complete absence of the diaphragm, and so to prolong life; but the individuals afflicted with this malformation have a second task to perform, namely, to put the abdominal wall on the stretch so that the inspiratory dilatation of the thorax may really be advantageous to the lungs. This, it is true, presupposes that the other muscles above named are intact and perfectly functional; and if, in the course of severe typhoid, the contractile power of the remaining muscles has decreased equally with that of the diaphragm, or if both diaphragm and intercostals are equally attacked by trichinæ, the intercostal muscles cannot vicariously perform the work of the diaphragm. In such cases the organism has recourse to *increased frequency of breathing*; instead of the deep and comparatively infrequent respirations, shallower but much more numerous ones are taken. The same thing occurs when the inspirations are cut short by pain and thus rendered shallow; this is one of the causes of rapid breathing in pneumonia, for example. Indeed, even when abnormal resistances impede respiration, there is an ultimate resort to increased frequency. Moderate obstacles lead first, it is true, to augmented action of the muscles, so that one not uncommonly finds in the emphysematous an actual *hypertrophy* of the scaleni, levatores costarum, and remaining muscles of the neck and chest, whose office it is to elevate the rigid and resisting thorax. But if, owing to the absolute strength of the abnormal resistance or to the insufficient muscular power, the obstacle cannot be overcome by such efforts, the breathing, as stated, becomes frequent. Thus, in a puerperal woman with extreme meteorism, 50 or 60 respirations may be counted, even when there is nothing morbid in the thorax. True, these respirations are *very superficial*; and, were the breathing not abnormally frequent, they would be far from sufficient to secure the physiological interchange of gases. Even so, the compensation by increasing the number of respirations is not perfect. The deeper portions of the lungs, in particular, are not supplied with air, and hence there is nothing more favorable to the production of *atelectases* than this mode of respiration. If you consider, moreover, that with such superficial inspirations, vigorous coughing with proper expectoration is impossible, it will be evident that, in such conditions, bronchial catarrh will only too readily develop, and, again, that splenisation and bronchopneumonia will often ensue on marked bronchitis.

The way in which the mode of respiration is altered when expiration is impeded is not unknown to you from former discussions. The most obvious resort, when the object is to overcome resistances, is the change of the *expirations* from being passive to *active*; *i. e.* the internal intercostals and, above all, the abdominal muscles contract vigorously. This change is, in fact, observed in the emphysematous, in whom expiration is wont to be decidedly prolonged and laboured. Still, you will not fail to notice that, as already pointed out, the insufficient expiratory diminution of the thorax must necessarily be attended by impaired inspiration. When, for example, the lungs do not normally retract, the relaxed diaphragm cannot become sufficiently arched, and the next contraction consequently fails to secure an adequate fresh dilatation of the thorax. Hence in these conditions the signs of an inspiratory dyspnœa must of necessity become associated with those of the expiratory dyspnœa; and in the more advanced degees of pulmonary emphysema one sees the unhappy patient employing all the accessory muscles of inspiration and expiration in the endeavour to appease his tormenting hunger for air. A similar state is produced by tonic cramp of the diaphragm, except that here superficial, but very frequent, hurried respirations are carried out, chiefly by the unaffected upper part of the chest-wall.

By means of this twofold regulation—reduction of the demand for oxygen and change in the mode of respiration—the organism has really the power of so compensating even considerable defects and deficiencies in the respiratory movements that the gaseous contents of the blood do not greatly deviate from the values indispensable for the maintenance of life. The utility of such regulation is of course most apparent in disturbances which pass off after a longer or shorter period, as *e. g.* in cramp of the diaphragm, as well as in many cases of meteorism, in trichinosis and in typhoid; for here the main object is to sustain life till the abdominal tension has abated, or the myositis has been removed, or the muscles weakened by typhoid have regained their strength—in short, till the normal conditions have been restored. But even in persons whose complete recovery is impossible this regulation is no less important, because by it a supportable, though not a perfectly physiological, existence may be maintained, not uncommonly for many years. If then the experiences we gained in connection with stenosis of the air-passages are repeated in the derangements now engaging our attention, it will be unnecessary to show that the power of regulation has its limits in the present instance also. For the consumption of oxygen cannot be reduced below a certain minimum, nor can the respiratory movements be modified, or increased in number, beyond certain limits. When, however, the boundaries of the regulative capacity are exceeded, the inevitable result is *asphyxia*, with the details of which we shall very soon have to occupy ourselves more minutely.

We now come to the third, and no less important, factor influencing the respiratory process, namely the *pulmonary circulation*. If, as we were able to assert, the exchange of gases between the atmosphere and the blood is to proceed regularly in the lungs, not only must fresh air constantly enter the alveoli, but fresh blood must be supplied to the capillaries, or, in other words, *the blood-stream through the lungs must be regular*. Now though we are pretty accurately acquainted with the anatomical arrangement of the pulmonary system of vessels, and in particular with the extremely rich and close network of capillaries, yet we have much to learn before we are sufficiently informed on all the details of the blood-stream itself: we do not even know whether normally the pulmonary capillaries are all constantly and equally filled with blood, or whether the blood-stream is unequally distributed over these channels. One thing is certain, however,—that, owing to the slight degree of resistance in the pulmonary circulation, the blood flows through the lungs under low tension but with no inconsiderable velocity, a velocity which is augmented at every inspiratory dilatation of the lungs. Undoubtedly such a flow is most advantageous to the exchange of gases in the lungs, and in fact the exchange goes on under these circumstances without interruption and with perfect regularity, provided the blood contains a sufficient number of red corpuscles, which, as is well known, absorb and fix the oxygen.

Derangements of the pulmonary circulation are, you are aware, some of the commonest occurrences in patholgy. I remind you of the processes, formerly discussed (vol. i, p. 101), by which smaller or larger *sections of the vascular system of the lungs are rendered impervious*. When branches of the pulmonary arteries are obstructed by thrombotic or embolic plugs, the capillary areas fed by them are almost lost to the circulation; as the result of cirrhotic processes large sections of the vascular system may be obliterated; where phthisical or bronchiectatic cavities are established the vessels must be destroyed, and even before cavities are formed by ulceration, the vessels within the caseous portions of the lungs must be rendered impervious by becoming involved in the necrosive process on which the caseation depends. We also stated on that occasion that with the destruction of the alveolar septa in pulmonary emphysema innumerable capillaries perish, and we also pointed out that all agents by which a lung is compressed and its natural volume reduced, such as large pleuritic exudations or tumours, and pneumothorax with high tension, must give rise to the occlusion of a more or less large number of vessels.

But even when the vessels of the lungs are pervious and undiminished in number, there is a number of processes by which the blood-stream through them may be impeded. Chief amongst them are those *cardiac lesions* in consequence of which either the motive power of the right ventricle is reduced, or the entrance of the blood of the pulmonary veins into the left ventricle is opposed by abnormal resistances. As you will remember from former discussions, the pulmonary circulation is impeded and consequently retarded in fatty degeneration of the right heart and in valvular lesions or aneurysms of the pulmonary, as well as in lesions of the mitral orifice and in extreme pericardial effusion; with this difference indeed, that in lesions of the first category the tension under which the blood flows through the lungs is abnormally low, while in the second, on the contrary, it is raised above the normal. If, moreover, the regular respiratory change in volume of the lungs is of considerable importance as a means of furthering the circulation, it is clear that anything which interferes with this change of volume must also impair the blood-stream through the lungs. Hence, as I pointed out on a former occasion, the pulmonary circulation suffers in *complete synechia of the layers of the pleura,* which prevents the lungs from gliding along the thorax towards the abdomen; and in this also consists one of the injurious effects of chronic *atelectasis* and of *chronic bronchitis,* since naturally the sections of lung, into which the bronchi plugged with mucus lead, cannot dilate during inspiration.

The total result to the flow through the lungs amounts, it is obvious, to the same thing in both cases. Whether the blood-channel be diminished, or the blood-stream slowed, owing to defective motive power or abnormal resistance, less blood must pass through the lungs and consequently less become saturated with oxygen, in the absence of means of compensating this disturbance. But you well know the means by which the organism is able to neutralise some of these evils, namely, the *augmentation of the work of the right ventricle,* which, if continuous, leads to its *hypertrophy.* The heart, acting more energetically and contracting more vigorously, drives through the smaller vascular channel as much blood as did the feebler contractions through the wider one, and in this way completely overcomes any obstacles that oppose the evacuation of the veins, so that, in spite of a mitral stenosis, the normal quantity of blood passes through the lungs in the unit of time. The flow of the blood is not, it is true, so perfect as in a normal condition, and in particular we must not under-estimate the importance of the fact that the tension in the pulmonary capillaries is necessarily raised in such cases.

That this factor should itself involve any interference with the exchange of gases between the blood of the capillaries and the air of the alveoli is certainly improbable. But there is developed, as is well known, under the influence of the permanent increase of pressure, not simply an ectasis but also a *thickening of the vessel walls*, which when affecting the large vessels is perceptible to the naked eye; and if this extends to the capillaries, it is evident that it must seriously impede the diffusion of gases. It is possible, then, that this circumstance may be no less responsible for the slight dyspnœa which, despite perfect compensation, is usually found in persons with mitral stenosis, than is the encroachment of the dilated capillaries upon the alveoli, to which Traube* repeatedly called attention. Nevertheless, no great weight appears to attach to this relationship; at any rate, if a number of twigs of the pulmonary artery be occluded in the dog by plugs of paraffin, there is usually nothing to indicate a disturbance of respiration; and in man, too, as is well known, the presence of non-irritating emboli in many pulmonary branches, even of high order, is not rarely an accidental post-mortem discovery, for which no symptoms *intra vitam* had prepared us. Similarly, it is usual for persons with synechia of the pleura, and even for the emphysematous, to enjoy good health, in spite of the loss of numbers of the capillaries, so long as they remain free from bronchial catarrh, by which the access of air to the remaining vessels would be interfered with. For the latter factor, the perviousness of the alveoli through whose capillaries the compensatorily augmented blood-stream passes, is obviously a necessary preliminary, in the absence of which the cardiac hypertrophy would be valueless to respiration. If they are pervious, one may count with tolerable certainty on the gaseous contents of the blood remaining within normal limits, provided the compensation of the circulatory disturbance is perfect.

Unfortunately, however, compensation is not always perfect. In the first place, there are some lesions, you are aware, which from their nature render an increase of the heart's work impossible, such, for example, as fatty degeneration of the right heart or large pericardial exudations. In a second series of cases, compensation fails because the derangement of the circulation is *absolutely* too great. This applies most evidently to direct occlusion of branches of the pulmonary arteries by thrombotic or embolic plugs. True, as regards this point, the experiments of Lichtheim formerly discussed have revealed the remarkable fact that a quarter the normal united sectional area is sufficient to allow the normal amount of blood to pass through the lungs. This, however, is the lowest limit beyond which the power of compensation fails; and the damage to the circulation cannot be averted by it, when more than three quarters of the pulmonary vascular system is rendered impervious by the occlusion of larger or smaller branches, or when the main arteries themselves are occluded. In the last place, you know that the compensation of the circulatory disturbance is still more frequently insufficient because the disturbance, though not *per se* irremediable, is so for the heart of the *affected* individual—because, in other words, it is relatively too great. In old, debilitated, or constitutionally feeble persons, or in those reduced by prolonged illness, a fairly good hypertrophy of the heart cannot develop. The existence of an older lesion similar to the recent one may also render the compensation of the latter impossible. Moreover, the functional power of a heart-muscle, which till a certain time has worked vigorously, or at least adequately, may after a longer or shorter period become exhausted, and the compensation will then of course be at an end.

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* Traube, ibid., ii, p. 308.

It need hardly be said that the occlusion of the main branches of the pulmonary involves the extinction of the circulation, and that the event is absolutely fatal. This accident or its equivalent, the occlusion of all the small pulmonary arteries, will consequently have less interest for you than the slighter disturbances in which, though life is not directly threatened, compensation is imperfect. We have already referred to the behaviour of the pulmonary blood-stream under these circumstances. For whatever the nature of the disturbance, whether a diminution of the blood-channel or a retardation of the flow, *the amount of blood passing through the lungs in the unit of time will always be reduced below the normal standard.* This applies equally to cardiac lesions, pleuritic exudations, and total synechia of the pleura, in all of which this result is averted solely by the compensatory hypertrophy. We have also referred to the consequences accruing to the exchange of gases in the blood; here also there is necessarily a *defect*. For while, owing to the retardation of the stream, the blood-corpuscles in the pulmonary capillaries can generally become thoroughly saturated with oxygen, yet you will not forget, on the other hand, that the same slow movement allows the blood very completely to dispose of its oxygen and to absorb carbonic acid in the systemic capillaries, so much so that in these cases the blood conveyed by the pulmonary arteries into the capillaries of the lung is much more venous than normal. But the apparent advantage is chiefly rendered illusory by the fact that an almost perfect saturation of the hæmoglobin with oxygen takes place even with the physiological more rapid flow. The fact consequently remains unshaken, that, in the unit of time, too small a quantity of oxygenated blood reaches the left ventricle, and through it the arteries of the body. The *medulla oblongata* is accordingly poorly supplied, and will react in the well-known manner to the deficiency of oxygen, not only by a sensation of shortness of breath, amounting it may be to intense dyspnœa, but by a dyspnœic strengthening of the respiratory movements. Persons suffering from uncompensated cardiac or pulmonary lesions are wont, if the affection is slight, to breathe more rapidly, even when at rest; while, when the disease is pronounced, they may present the pitiable picture of extreme dyspnœa or even complete orthopnœa. So much is this the case, that in total occlusion of the pulmonary arteries by emboli, the affected individuals perish with no other symptoms than those of the most agonising hunger for air.

But of what utility, you will ask, are the strengthened dyspnœic respiratory movements to these patients? For even one who is completely imbued with the idea of the mechanical necessity of this dyspnœa will, in view of the extremely ingenious contrivances of our organism, seek amid all their complexity to discover some indication of a compensatory arrangement in the effects brought about by a disturbance. Here, however, where blood is wanted in the capillaries, and not air in the alveoli, of what use is it that the increased action of the respiratory muscles conveys larger quantities of air into the lungs? If, as a matter of fact, the dyspnœic respiratory movements simply conveyed an increased amount of air into the alveoli, and did no more than this, we should be compelled to agree with Filehne,* who has characterised the dyspnœa of persons suffering from heart-disease as perfectly useless, in a remarkable paper lately published. In reality, however, they exert an important effect in quite another direction, namely, *by furthering the pulmonary circulation.* If even the ordinary respiratory changes of volume increase the velocity of the blood-stream through the lungs, still more will this be the case with the forced and consequently more ample and numerous dyspnœic alterations. The respiratory movements in dyspnœa are consequently an excellent means of augmenting the velocity of the pulmonary circulation, and, when this is from any cause abnormally reduced, of rendering it possible for an approximately normal amount of blood to flow through the pulmonary capillaries in the unit of time. They are, therefore, by no means to be despised as means of compensating the loss of some of the blood-vessels of the lungs; and though, of course, they cannot restore the lumen of an occluded artery, they contribute not a little, as I formerly (vol. i, p. 218) pointed out, to convey blood from the neighbouring territories into the capillaries situated beyond the occlusion. An increase of the amount of blood flowing through the lungs means simply an increase of the oxygen, and diminution of the carbonic acid, contents of the blood; and the dyspnœa thus proves to be a means of regulation not only in interference with the access of air, but in disturbances of the pulmonary circulation.

We arrive at similar conclusions on considering the influence which is exerted on the respiratory process by *blood of abnormal constitution.* True, we need not here consider all changes in the composition of the blood; for, obviously, only such of its morbid conditions can be of importance to respiration as either disturb the blood-stream or diminish the number of healthy red blood-corpuscles present in it. Both these results occur in *cholera*, in which, owing to the extreme condensation of the blood, the entire circulation is retarded enormously, while that the red corpuscles are seriously damaged is sufficiently testified to by the passage of the potash salts into the plasma. Further, with regard to the second point, I may remind you of the various forms of essential or secondary *anæmia* and *oligocythæmia*, discussed in the first section, which, however greatly they differ in other respects, agree in this—that the number of functional red corpuscles contained in the blood has more or less decreased. The consequence to the interchange of gases in the blood may easily be defined. For if the red corpuscles with their hæmoglobin, while passing through the pulmonary capillaries, absorb oxygen from the alveoli and saturate themselves with it, every reduction of the hæmoglobin-contents of the blood must necessarily be followed by a falling off in the amount of oxygen also. That this is the signal for the setting up of dyspnœic breathing I need hardly say; and it is only necessary to point out that the strengthening and increase of velocity of the pulmonary circulation in consequence of the dyspnœa is an indubitable means of regulation in these cases. For if the error here consists in the presence of too small a quantity of oxygen in a determinate quantity of blood at a given moment, this evil can evidently be compensated, at least to a certain extent, by increasing the blood-quantum itself.

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* Filehne, 'A. f. exper. Pathol.,' x, p. 442, xi, p. 45.

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CHAPTER III.

DYSPNŒA AND ASPHYXIA.

The frequent combination of different impediments to respiration.—The physiological exchange of gases in the blood.—Limitation of the oxygen-consumption in respiratory lesions.—Regulation by dyspnœa.—Gaseous contents of the blood in the respiratory lesions.—Limitation of the oxidative processes.—Cyanosis.—Other effects of the respiratory lesions on the circulation.

Impossibility of regulation owing to the absolute amount of the impediment.—Acute asphyxia.—Explanation of the phenomena of asphyxia.—Slow suffocation.—Its causes.—Gradual increase of the impediments to respiration.—Decreasing functional power of the respiratory muscles.—Diminished irritability of the respiratory centre.—Cheyne-Stokes respiration.—The blood-gases in slow suffocation.—Carbonic-acid poisoning.—Post-mortem appearances in asphyxia.

As you have gathered from the preceding discussions, the morbid processes producing disturbances of respiration are extremely numerous, and although they are all at bottom dependent either on interference with the access of air to the respiratory surface, or on irregularity of the pulmonary circulation, yet they differ much in nature. At the same time it will not have escaped you that we have repeatedly considered the same process on different occasions, thus implying that one and the same factor is capable of impairing respiration in several directions—an experience the like of which we also had formerly, *e. g.* when considering the pathology of gastric digestion. A large pleuritic exudation not only renders many of the alveoli inaccessible, but compresses numbers of the pulmonary capillaries, and gives rise to shallow respiration, at least on the affected side; an extensive bronchitis obstructs the passage of air to the alveoli, and also the blood-stream through the affected portions of the lungs; a pneumonia occludes the alveoli, as far as the infiltration extends, and, owing to the accompanying pleuritic pain, it renders the breathing superficial; and in emphysema of the lungs the impairment of the pulmonary circulation through the destruction of so many of the capillaries is associated with the impediment to respiration resulting from the considerable decrease of elasticity of the lungs, to which there is often added a rigidity and immobility of the thorax. While, accordingly, individual pathological processes are not uncommonly attended by several dangers to respiration, which are the more threatening from their concurrence, this is still more the case when, as only too often happens, a number of different prejudicial factors assert themselves during one and the same disease. One of these factors may follow immediately on another, in the sense that one disturbance gives rise to the other directly. This happens *e. g.* when laryngeal croup becomes complicated by bronchitis and broncho-pneumonia, in other words, a stenosis of the larynx and trachea by a narrowing of the bronchi and the occlusion of numbers of alveoli; or when a patient with stenosis of the left auriculo-ventricular orifice gets a hæmoptoic infarct, and to the increased tension and slowing of the pulmonary blood-stream there is added imperviousness of some blood-vessels and occlusion of many alveoli. Yet such a causal relationship is far from always occurring in these complications. If a person having phthisical cavities in his lungs gets embolic occlusion of some of the pulmonary arteries owing to thrombosis of the veins of the leg, only a very remote causal connection can be said to exist here; moreover it is always an accident, though a frequent one, when a person whose pleura is adherent and certain sections of the lung atelectatic or an emphysematous individual gets bronchitis. Also when, in a puerperal woman or in the course of typhoid, bronchitis and meteorism and feebleness of the respiratory muscles concur, we can at most say that all these disturbances are co-effects of a common cause, not that one of them is conditioned by another. But whatever the mutual relation of these accumulated evils, new points of view are not presented by such complications. For their action is the same in every case, in that they all interfere with the physiological interchange of gases in the blood, so that their combination has the same importance simply as *a quantitative increase of any one of them* would have, and their effect on the interchange of gases must amount to this—a higher degree of diminution of the oxygen, and augmentation of the carbonic acid, contents of the blood.

The oxygen contents of arterial blood, *i. e.* the absolute amount of oxygen contained in the blood, varies, as is well known, normally, not merely in different individuals but in the same person. Thus, for example, the values determined on perfectly healthy dogs considerably exceed and fall below the average of 17 vol. per cent. (calculated at 0° and 1 m. pressure) found to prevail in the blood of the dog's carotid. These deviations are due to the varying contents of the blood in hæmoglobin, with which substance almost the whole of the oxygen enters into combination, and whose amount consequently is exactly proportional to the oxygen stored up. The hæmoglobin is almost completely saturated in the lungs and the blood leaves them almost as rich in oxygen as it is possible for it to be, and it is such blood that is carried at all times by the arteries into the organs of the body, which necessarily require a copious stream of oxygen for the maintenance of their regular metabolism and the discharge of their various functions. This feature—the almost perfect saturation of the blood with oxygen, and not the absolute amount of the oxygen stored up, is the criterion of a regular interchange of gases in the blood. But since a more or less large amount of oxygen is being constantly withdrawn from the blood in the various organs of the body, so that the venous blood returns to the heart from ¼ to ⅓ poorer in oxygen, the saturation of the arterial blood would be rapidly at an end, were not the consumed oxygen most promptly replaced in the lungs. In a normal condition, the most perfect accommodation prevails between consumption and replacement, between oxygen-expenditure and oxygen-income. If the consumption is slight, *i. e.* if the venous blood on its return to the lungs is comparatively rich in oxygen, the continuous though slow diffusion between the air of the alveoli and the atmosphere goes a great way towards saturating the blood of the pulmonary capillaries with oxygen, and a moderate acceleration of the air-stream to the alveoli by means of the respiratory movements is certainly all that is necessary in addition. It is not so when the consumption is great. The venous blood then becomes so poor in oxygen that the normal proportions cannot be restored without the absorption of very large quantities of this gas; extensive respiratory movements come to the aid of diffusion, and, on the one hand, rapidly remove the useless residual air from the alveoli and convey large supplies of fresh air into contact with the surface of the blood-capillaries, while, on the other, they powerfully augment the blood-stream, so that in a brief interval a much greater amount of venous blood than ordinarily is exposed to action of the air. Thus the absorption of oxygen follows directly and promptly on consumption; but the converse regulation, *i. e.* the regulation of the consumption according to the amount of income, does not practically come up for consideration in a physiological condition. For with regard to the question how the organism behaves towards a possible augmented oxygen supply, I stated recently, and after to-day's discussion I am in a still better position to remind you, that this possibility is simply set aside by the fact that arterial blood is normally almost completely saturated with oxygen. As regards the carbonic acid—to which the considerations just dwelt on are equally applicable, though in an opposite direction—it is not to be denied that a voluntary augmentation of the respiratory movements aids in its excretion; yet these same respiratory movements more than sufficiently secure that there shall be no dearth of this gas in the blood. While an abnormal increase of the oxygen-supply is feasible only within very narrow limits, its abnormal diminution is not only easily conceivable, but plays a very real and most important *rôle* in the pathology, though not in the physiology, of respiration.

For here belong all those respiratory lesions so thoroughly discussed by us, which, whether interfering with the access of air to the blood or of the blood to air, are respiratory lesions only in virtue of the fact that they diminish the absorption of oxygen and the excretion of carbonic acid. Is this reduced absorption of oxygen compensated for by an equal reduction of the consumption? Certainly it is; for, as I have told you repeatedly, persons suffering from such respiratory affections consciously or instinctively behave so as to limit as far as possible their consumption of oxygen and production of carbonic acid. Still they cannot accomplish much in this way. For however greatly they may restrict their muscular movements and however rationally select their food, oxygen consumption and carbonic acid production cannot, while life lasts, fall below a certain minimum. Consider besides that no one can permanently avoid employing muscles other than those which are absolutely necessary to life, and it will be obvious that sooner or later a moment must arrive for these individuals also, when the income and expenditure of oxygen do not cover each other, the former falling short of the latter. Under these circumstances the same condition appears, which, with a normal oxygen supply, is the consequence of an abnormally abundant consumption; and the response of the organism will therefore be the same. In fact, I have already dwelt on *dyspnœa* as the constant result of all the respiratory lesions. True, the form in which the dyspnœa manifests itself differs. For though it is correct that we understand by dyspnœic respiration, an augmentation of the respiratory movements as regards depth and number, it is very far from correct that the deepening and increased frequency of the respirations coincide in every case. Rather I have felt it to be incumbent on me to educe the conditions under the influence of which, in each individual respiratory affection, the breathing becomes at one time deeper and slower, at another more frequent and shallow; and to explain why on one occasion inspiration, on another expiration, is laboured and carried out with the aid of all the accessory muscles, and how it happens that in one case all the inspiratory muscles, and in another only some of them, energetically participate. This appears to me to be one of the most attractive sides of the study of the respiratory derangements, namely, the discovery of the ways and means adopted by the organism, in presence of these very different lesions, with a view to bring about that modification of the respiratory movements which shall, in the particular case, be most advantageous, most remedial. It is because it effects this that the dyspnœic breathing becomes what I have so often called it—*a means of regulation*. For if in these lesions, the absorption does not equal the consumption of oxygen, it is not because the blood has lost its ability to absorb more oxygen, but solely because of the inadequate contact of the blood and air at the respiratory surface; and the dyspnœic breathing, by now providing for the abundant flow of both, air as well as blood, towards the surface, can compensate the pernicious effects of the diverse lesions.

But how do the *gaseous contents of the blood* behave under the influence of the dyspnœa in our respiratory lesions? To answer this question with sufficient accuracy it would be necessary to have what, so far as I know, we are absolutely unprovided with—analyses of the gases contained in the blood of persons, or at any rate animals, suffering from disease of the respiratory organs. This is certainly a great and lamentable deficiency in our knowledge, to meet which we are compelled meanwhile to rely solely upon hypothesis. Still our guesses are supported not merely by the results of investigations into the physiological interchange of the gases of the blood, but by certain symptoms so manifest that we shall hardly be likely to wander very far from the truth.

The almost complete saturation of the arterial blood of a healthy man with oxygen, occurring during ordinary respiration, depends on the fact that a certain fraction of the blood —the quantity passing through the pulmonary capillaries in the unit of time—or the red corpuscles contained in it, constantly become saturated with this gas. When now, owing to the imperfect access of air to the alveoli, a portion of the blood-corpuscles contained in this quantity does not become saturated, or when, as in the uncompensated cardiac lesions, the quantity itself is reduced, the inevitable result must plainly be that the oxygen-contents of the arterial blood will fall more or less considerably short of the point of saturation: by how much, evidently depends on the degree of the impediment to respiration. And how is this condition affected by the dyspnœa? Now, by the dyspnœic breathing every respiratory lesion may be compensated within certain limits, the more trifling ones by a slight strengthening or numerical increase of the respirations, the severer by a correspondingly forced exertion of the respiratory muscles. Are then all individuals who suffer from any respiratory lesion continually in a condition of slight or more pronounced dyspnœa? Far from it: on the contrary, persons afflicted with kyphosis, with chronic bronchial catarrh, with extensive pleural adhesions, or with moderately severe emphysema, and even patients with bronchiectases or cavities of not unduly large dimensions, do not usually display any essential differences in their breathing as compared with individuals of the same age and sex, so long as they remain quietly seated or lying. On the other hand, dyspnœa is scarcely ever absent in extreme emphysema, in advanced phthisical changes, in extensive acute pneumonia, in acute general tuberculosis, in pleuro-pneumonia before the crisis, and may attain its highest conceivable degree in croup, in stenosis of the trachea due to compression or bending, and in pneumothorax, &c. Such being the case, the dyspnœa cannot be due solely to the simple fact of imperfect saturation with oxygen, for the arterial blood is not saturated in normal fashion in the slighter respiratory affections; it evidently depends on *the degree of the oxygen-deficiency*. But in seeking to discover what degree of poverty in oxygen must exist before the dyspnœa begins, we shall not be likely to go far astray if we regard the relation of the income to the expenditure as the determining element here also. In the slighter impediments to respiration, ordinary breathing does not, it is true, secure the normal degree of saturation of the arterial blood; the organs are consequently supplied with blood whose oxygen contents are less than normal, while the blood of the veins is more than normally impoverished as regards this gas. Still the ordinary quiet breathing is capable of conveying as much oxygen to the blood as was lost from the capillaries of the body, and in this way there is established a permanent equilibrium of the arterial gaseous contents, which, it is true, *remains below the level of physiological saturation*. In the more serious respiratory lesions, on the contrary, only a small quantity of oxygen reaches the blood during ordinary breathing, and not only is the physiological saturation of the blood not secured, but the continuous loss of oxygen to the organs of the body is not covered. Here, therefore, instead of a condition of equilibrium, the consequence would be a gradually increasing impoverishment of the blood in oxygen, which would soon be incompatible with life, did not the dyspnœa step in to aid. A completely normal saturation of the blood with oxygen is not usually the result of the dyspnœa in such patients, though it is quite within the bounds of possibility. For if you consider what uninterrupted laboured breathing involves, and reflect further that the increased work of the respiratory muscles itself makes additional demands on the respiratory apparatus by augmenting the production of carbonic acid, you will think it conceivable enough that the dyspnœa of these patients should not usually exceed the degree necessary to the maintenance of life, or in other words, the amount sufficient to cover the deficit in the income compared with the expenditure of oxygen. The dyspnœa is indispensable to individuals with considerable impediments to respiration, because they could not continue to exist without it; but it does not put them on the same footing with healthy persons as regards the gases of the blood, but merely provides for the establishment of that lower state of equilibrium which, in the complete absence of dyspnœa, is usually found in patients afflicted with the slighter respiratory lesions.

It is anything but a matter of indifference, however, whether the arterial blood is properly saturated with oxygen or not. How unenviable is the position of persons with the low condition of equilibrium, is at once apparent on the slightest disturbance of this condition. Our organism is accustomed to command an abundant supply of oxygen, and we can walk at a fair rate or go through other respectable bodily exertion, and can consume large quantities of food containing carbohydrates without any resulting dyspnœa. Observe, on the other hand, a person whose store of oxygen is small, and whose ordinary, or, it may be, dyspnœic respiration just suffices to cover the indispensable consumption of oxygen, even though this has been reduced as far as possible; on walking a few yards or mounting stairs, the breathing of a person with pleural adhesions becomes short, and the phthisical or emphysematous individual develops marked dyspnœa. This is the reason, too, that the accompanying pyrexia can so considerably enhance the dyspnœa of a patient suffering from an affection of the lungs. The accession of an impediment to respiration, which, in itself slight, would be productive of only trifling inconvenience to a healthy person, is often sufficient to cause the most violent dyspnœa in one who is already the subject of a considerable respiratory lesion. Precise numerical values cannot, it is evident, be given here, if for no other reason because the individual circumstances must be taken into consideration. For hardly on any other occasion is the capacity of the organism to accommodate itself to altered conditions displayed in so clear a light. It is not merely that, as more than once stated, persons with impediments to respiration instinctively limit as far as possible the expenditure of oxygen which is subject to their control; the *oxygen used up in the metabolism of the various organs independently of volition* is also diminished. This does not occur in the way which, on the ground of inadequate evidence, met with much acceptance formerly, when it was believed that some of the nutrient and tissue materials were not converted into the final waste products, so that instead of these a number of less highly oxidised substances appeared in the excretions. Rather, as was first definitely determined by Senator,* the regular course of the oxidative processes remains undisturbed under these circumstances; there are no qualitative deviations from the normal, but less is undertaken generally, so that the entire metabolism is reduced, as happens in inanition. It would make no difference in this respect, were the rule laid down by Fraenkel, according to which the decomposition of albumen increases with diminution of the oxygen-supply (cf. vol. ii, p. 672), universally applicable; for this has nothing to do with the oxidative processes, with which alone we are concerned here; and if, as we formerly declared to be probable, the fat so separated remains lying unconsumed, this is only a welcome confirmation of the above proposition. Nevertheless, the organism needs a certain time in which to adapt itself to the scanty store and supply of oxygen, and herein we may certainly see a reason for the fact that the same respiratory impediment which, when suddenly attacking an individual previously healthy, produces extreme dyspnœa, should gradually become tolerated by the patients, who then suffer no very great respiratory trouble.

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* Senator, 'Virch. A.,' xlii, p. 1.

That in persons suffering from impediments to respiration, the oxygen contents of the arterial blood actually fall more or less short of the physiological point of saturation, has not, as already stated, so far been determined by analysis; yet it is, in my opinion, convincingly demonstrated by a symptom, no less often present in diseases of the respiratory, than in affections of the circulatory, apparatus. I mean *the bluish coloration of the skin*, or to employ the *terminus technicus*, the *cyanosis*. The bluish hue depends, as you will recollect from former discussions (vol. i, p. 32), on the fact that the blood circulating in the capillaries of the skin parts more completely with its oxygen and takes up more carbonic acid than usual, and so acquires more distinctly venous characters than under physiological conditions. But while, in the uncompensated cardiac lesions and other general disturbances of the circulation, it was the retardation of the blood-stream that favoured the development of cyanosis, in the impediments to respiration, the diminished oxygen contents of the blood, even before it has entered the capillaries, must be regarded as its cause; in a number of respiratory lesions, however, both factors coincide, the reduced velocity of the blood-stream and the diminution of the arterial store of oxygen. The degree of cyanosis may vary extremely, and while, in the slighter respiratory impediments, it is hardly perceptible, in croup, in œdema glottidis, in acute catarrh of all the bronchi, &c., it may attain its highest pitch, so that the entire surface of the body acquires a decided and pronounced blue coloration. But the development of marked cyanosis is often prevented by a condition of general anæmia. Thus, to the hectic fever and the general emaciation we must ascribe the fact that in ordinary phthisis, despite the advanced disease of the lung, the patient appears pale and not cyanotic; and that the absence of cyanosis is not due to the tubercular nature of the affection is most clearly shown by the intensely deep hue of the skin, which is so regularly observed in acute general miliary tuberculosis as to constitute one of its differentially diagnostic symptoms.

I may take this opportunity to point out that the circulatory apparatus is variously influenced by the respiratory lesions, quite apart from the occurrence of cyanosis and of hypertrophy of the right heart, so often the subject of discussion. Every loss of elasticity of the lungs necessarily weakens the suction of the thorax, and thus impedes the entrance into it of the venous blood. A still worse effect of the same kind is produced by forced expiration, owing to which the negative pressure of the thorax is converted into a positive one. Since, however, both these factors concur in extreme emphysema, in which too the united sectional area is reduced by the loss of innumerable capillaries, you will not be surprised to learn that all the consequences of uncompensated circulatory lesions may set in in such patients. You know also that the overloading of the blood with carbonic acid exerts a stimulating effect on the vaso-motor centre, and I may remind you that, following Traube, we made use of this fact to explain the hypertrophy of the *left* heart which occurs in many pulmonary lesions (vol. i, p. 97). But note well in this connection that the vaso-motor constriction of the small arteries involves those of the body alone and not those of the lungs, so that the greater amount of blood which, owing to the increased arterial pressure, flows from the veins to the heart, reaches the pulmonary capillaries without any diminution or impediment. On the other hand, this richness of the blood in carbonic acid acts at the same time as a stimulus to the vagus centre, so that in considerable respiratory impediments the pulse-rate is not uncommonly retarded —evidently a highly advantageous arrangement, in view of the fact that every reduction in frequency of the pulse involves the like reduction in the working phases of the heart, and thus diminishes the demand for oxygen, of which such patients have anything rather than a superfluity.

Despite the impairment of so very important a function, persons suffering from respiratory diseases can yet, as we have seen, sustain life, and that often for a really long time. They differ from healthy persons, it is true; still in less severe cases there is not even continuous shortness of breath, though in extreme ones life is preserved only by the interrupted dyspnœa. Yet the organism gradually accustoms itself to this— provided at least it does not exceed moderate bounds. For the most intense degrees of dyspnœa, in which the demand for air can be met only by the most violent action of all the inspiratory and expiratory muscles, *cannot possibly be permanent*, because the functional power of the respiratory muscles would sooner or later be exhausted. In the respiratory lesions of slight and moderate severity, the paroxysms of air-hunger fortunately pass off rapidly, so that the extreme dyspnœa is only temporary; while the danger of the severe respiratory impediments lies in the fact that they can be compensated, or at least rendered tolerable, only by the most extreme dyspnœic efforts. That a person can at all recover from laryngeal croup, from acute diffuse bronchitis, or from œdema of the lungs is due simply to the intense dyspnœa; and yet—is it not really superfluous for me to call attention to the important place occupied by respiratory diseases in the death-returns of our race?

The causes of this are easily discovered. In the first place, an impediment to respiration may be so *considerable*, that the means of regulation at the organism's disposal are powerless to overcome it. A person whose trachea is constricted by a rope or by the hand of a strangler may breathe with as much effort and with as many muscles as is possible; but he will convey no air to his alveoli. Or, to choose an illustration from the domain of pathology proper, when all the alveoli are flooded in a short time with liquid, when a large quantity of blood suddenly pours from a ruptured artery into the bronchial tree and flows through all its ramifications, what avails the most violent dyspnœa? And how can an animal help itself by dyspnœa if the increase in volume of the thorax is rendered impossible by an elastic bandage, or if the respiratory muscles are paralysed by curare? Lastly, how can the most laboured breathing and the most extreme augmentation of the work of the right ventricle avert, or ward off for a time, the fatal effect of complete embolism of the pulmonary arteries, either of the main trunks or of all the smaller branches? Under such circumstances, in fact, there is invariably developed a group of phenomena, which cause death more or less rapidly, and which we are accustomed to embrace under the designation *asphyxia* or *suffocation*.

It is a stormy scene enough that follows the sudden closure of the cannula placed in the trachea of a rabbit, or the compression of the trachea itself. The breathing at once becomes long-drawn and extremely laboured, and at each inspiration the nostrils are actively dilated, while soon the mouth is thrown widely open, the neck stretched out, and the head bent backwards. The animal now becomes very restless; in its hunger for air the head is turned at one moment in one direction, the next in another, as it incessantly gasps anxiously for breath, till, the restlessness becoming greater and greater, *convulsions* set in. At first slight twitchings occur, but these rapidly increase in severity, and develop into the most violent general spasms, by which the rabbit, unless it is held, may be tossed high into the air and thrown to a distance. These clonic convulsions do not last long, but give place to a state of complete insensibility and paralysis, in which the animal lies with protruding eyeballs and dilated pupils. For a time the breathing is perfectly arrested, till a few hurried, broken respirations, becoming gradually more and more feeble, announce the near approach of death. This whole series of phenomena occupies but a few minutes. If during it the carotid of the rabbit be kept connected with the kymograph, a rise of arterial pressure is detected very soon after the beginning of the dyspnœa; the increase of tension may be very great, to 150—170 or even 180 and more mm. mercury; and only *in the stage of asphyxia*, *i. e.* after the convulsions have ceased, does the mercury begin to fall, and now rapidly approaches the abscissa. Yet for a considerable time after the last inspiration the pressure continues positive, and the elevations of the curve occasioned by the systole of the heart only gradually disappear; in other words, *the cardiac contractions in asphyxia persist for a certain time after the respiratory movements have ceased*, it may be for two or even three minutes. While the arterial pressure was still high, you noticed on the curve those large and slow pulsations, with which you are familiar under the name of vagus-pulsations; and it is precisely here, on the curve of asphyxia, that the truth of my statement with regard to the utility of the stimulation of the vagi by the dyspnœa is most evidently demonstrated, for if the vagi be divided before occluding the chea, the asphyxia apparently sets in more rapidly in some animals, and certainly the heart invariably becomes much more speedily paralysed than with the vagi intact.

The explanation of all these phenomena is found in the alteration of the gaseous contents of the blood. From the moment when, owing to the occlusion of the trachea, fresh air containing oxygen no longer reaches the pulmonary capillaries, to cover the consumption which still continues, the blood must rapidly be impoverished in oxygen, and, because of the impeded excretion, will become loaded with carbonic acid, so that the blood contained in the arteries will very shortly surpass ordinary venous blood in both these respects, and will in fact appear much darker than it. Blood of this nature not only excites the centre for the respiratory movements—hence the extreme dyspnœa—but the stimulus will extend, with the increasing impoverishment of the blood in oxygen, still more widely through the grey matter of the medulla; the vaso-motor centre and then that of the vagus will be excited, and finally centres which are stimulated with greater difficulty—that for the dilatation of the pupils and the so-called *convulsive centre*—become implicated, the latter being an area situated in the medulla oblongata by whose stimulation almost the whole of the voluntary muscles may be thrown into violent contraction. The factor lending the blood in asphyxia this eminently stimulating property does not admit of doubt; it is *the deficiency of oxygen*. The question, at time so energetically discussed, whether dyspnœa is due to the dearth of oxygen or to the accumulation of carbonic acid, has been decided, as you will remember from your physiological studies, in this sense, *that either may be the cause of the augmented respiratory movements*. In the dog, the respirations become deeper and more frequent when the animal is made to breathe a mixture of gases in which there is present as much, or more, oxygen than in the atmospheric air, together with a great excess of carbonic acid, in which case the saturation of the arterial blood with oxygen is not interfered with, while the blood is overloaded with carbonic acid. But the dyspnœa appears with equal promptness when the blood of the dog is rendered poor in oxygen, either by the respiration of pure nitrogen, or of a mixture of gases in which oxygen is deficient; and this occurs even when the accumulation of carbonic acid in the blood is completely prevented[*] by its continued absorption from the space in which the animal breathes. But though this is perfectly correct, it is utterly impossible that an animal could be killed in a few minutes even by the most enormous accumulation of carbonic acid in the blood. Pflüger[*] observed dogs with more than 50 per cent. carbonic acid in the blood, which, though dyspnœic, were quite lively so long as the store of oxygen was normal, and values such as this are not even approached in suffocation by occlusion of the trachea. The abnormal accumulation of carbonic acid in the blood is followed, as you know, by slowing of the pulse and rise of the blood-pressure, yet the latter does not reach such a height nor persist so long as after occlusion of the trachea, and above all there never occur in carbonic-acid poisoning those violent convulsions which invariably accompany acute asphyxia. No; death by rapid suffocation is the effect solely of the poverty in oxygen, the loss of which takes place so rapidly that, in healthy and strong dogs breathing an atmosphere of pure nitrogen, Pflüger witnessed a fall of the oxygen-contents of the arterial blood in thirty to forty seconds from the normal saturation-values (15, 17, and 18 per cent.) to 2·6 and even to 1·5 per cent. Under these circumstances, you perceive, only very minute quantities of oxygen are conveyed by the arterial blood to the medulla, and when for any cause the oxygen contents of the cerebral areas in question rapidly fall to a minimum, they react in the manner described. Hence precisely the same phenomena, appearing in the very same order as in asphyxia, set in upon rapid and very copious bleeding, further in the acute cerebral anæmia produced by Kussmaul and Tenner by occluding the carotids and vertebrals, and lastly in complete and sudden obstruction of the venous efflux.[†] In all these cases the same dyspnœa, rise of arterial pressure, and convulsions occur, and in all of them these violent signs of irritation are not attributable to the mechanical disturbance of the blood-stream, but, as conclusively demonstrated by Rosenthal,* to the acute change in the gaseous contents of the cerebral areas, *in specie* to their rapid loss of oxygen. These stormy symptoms constitute in a measure the alarm-cry of the organism, announcing the approach of extreme danger; for if blood rich in oxygen be not rapidly supplied to the central organ, the irritability of the latter ceases, consciousness is lost, motility and sensibility are destroyed, and the cerebral centres fail to react to any kind of stimulus; the heart, the function of which also depends on the presence of oxygenated blood, soon stands still, and death takes place. In the blood which still circulates during asphyxia, no distinction of colour can be made out between the arteries and veins; it is everywhere almost perfectly black, although it contains slight traces of oxygen removable by the pump, and shows the absorption-bands of oxyhæmoglobin;† after death has occurred, however, the last vestige of oxygen quickly disappears. But the blood of asphyxia has not lost its capacity of absorbing oxygen, and hence, while the heart continues to beat, life may be saved by artificially conveying air rich in oxygen to the pulmonary capillaries. Twitchings of different muscles are usually the first sign of reawakened irritability; the artificial insufflations are interrupted first by occasional and afterwards by more frequent dyspnœic inspirations; meanwhile sensibility and movement have returned, and the animal soon raises itself and thenceforward breathes, moves, &c., in a perfectly normal manner.

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[*] Cf. the important paper on this subject by Pflüger, his 'Archiv,' i, p. 61. Amongst the most recent literature cf. especially Friedländer und Herter, 'Zeitschr. f. physiol. Chemie,' ii, p. 99, iii, p. 19, contains numerous references. Further, P. Bert, 'Leçons sur la physiologie comparée de la respiration,' Paris, 1870; 'La pression barométrique,' Paris, 1878.

[†] Hermann und Escher, 'Pflüg. A.,' iii, p. 3.

Human pathology does not often afford us an opportunity of observing death by acute asphyxia. The complete and sudden occlusion of the main branches of the pulmonary artery can scarcely be cited as an example of pure death by asphyxia, since this accident at the same time causes a sudden interruption of the entire circulation. Here death usually takes place still more suddenly than in suffocation, and no time is left for the development of violent dyspnœa or of general convulsions; the patient gasps a few times anxiously for air, the body is bent in opisthotonus, and then immediately sinks down deprived of sensibility and consciousness, and all is over. Typical and uncomplicated examples of death by asphyxia are afforded by fatal *spasm of the glottis*, and by the sudden bending of the trachea occurring in persons suffering from goitre. Further, when death occurs in a few minutes, after the escape into the air-passages of a large quantity of blood from a ruptured vessel, it takes place with all the phenomena of asphyxia; thus *e. g.* a fatal hæmoptysis in a phthisical subject almost invariably causes death by suffocation and hardly ever by the loss of blood. Lastly, in those rare cases where an already existing unilateral pneumothorax becomes complicated by pneumothorax on the opposite side, perhaps owing to the rupture of a phthisical cavity, life is rapidly terminated by suffocation. Many more illustrations of death by acute asphyxia can hardly be selected from pathology. For several other processes, though in themselves acute, do not so abruptly terminate respiration as to justify us in speaking of acute asphyxia; thus hours may pass before a patient succumbs to œdema of the glottis or to a paroxysm of pulmonary œdema, and death from croup is usually preceded by an illness of several days, *i. e.* by a stenosis of the larynx of several days' duration. And now as regards pleuropneumonia, bronchitis, pleuritic exudation, trichinosis, pulmonary emphysema and pulmonary tuberculosis—who does not know that persons ultimately dying from one of these diseases of the respiratory apparatus are previously for days and weeks, or indeed months, the subjects of more or less considerable disturbance of the respiratory process?

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* Rosenthal, 'A. f. Anat. u. Physiol.,' 1865, p. 191.

† Stroganow, 'Pflüg. A.,' xii, p. 18.

If an individual suffering from any one of these diseases actually perishes from the impediment to respiration, this invariably implies that the alteration in the gaseous contents of the blood—the diminution of oxygen and the increase of carbonic acid—has become so considerable that life has ceased to be compatible therewith. It is obvious that in this gradual deterioration of the gaseous contents, this *slow* suffocation, no such obstacles can exist as exceed from the start the regulatory capabilities of the organism. But there are many impediments which increase gradually, and which, after being for a certain period more or less completely compensated, at first by moderate and then by extreme dyspnœa, may finally reach such a pitch that the strongest dyspnœa can no longer postpone the fatal impoverishment of the blood in oxygen. It is in this way that œdema of the larynx and of the lungs, and very often laryngeal croup, prove destructive; in this way also pneumonia proves fatal when it successively involves larger and larger portions of both lungs; and in the same category must be placed those cases—not indeed frequent—where death occurs because the smaller pulmonary arteries are occluded one after another by ordinary bland emboli. I may remind you, further, of a remark we formerly made as to the frequency with which a respiratory lesion becomes complicated, either as a natural consequence or quite independently, by a fresh impediment to respiration, of such a kind that the degree of dyspnœa of which the individual concerned is capable, no longer suffices to secure compensation. The individual concerned, I say, for here we meet a further factor of extreme importance as regards the question now engaging our attention, namely, that the power of regulation is not equally great in all persons or in the same person at different times. If, on division of both the phrenics, a very young rabbit at once dies from asphyxia, while an older animal usually survives the operation for days and weeks, this difference is attributable simply to the fact that the weak scaleni, intercostals, levators, &c., of the young animal are not yet capable of effecting the inspiratory dilatation of the thorax necessary to sustain life, a task which the stronger muscles of the fully grown animal can accomplish without difficulty. To secure the actual *strengthening* of the respiratory movements in dyspnœa, the first and indispensable condition is *that the respiratory muscles should be functional and vigorous.* True, we were able to make out that the organism can compensate for the excessive feebleness or too small extent of the respiratory movements by increasing their frequency; but, if the respirations are to continue to subserve the interchange of gases, this increase of frequency has its limits; and then of what avail is the multiplication of the respirations, with the shortening and shallowness inseparable from it, as against a stenosis of the larynx or trachea, a diffuse bronchitis, an extensive atelectasis, in short, against any of those respiratory impediments, which can be compensated only by a lengthening and deepening of the respirations, and to which the body is accustomed to respond by this modification of the respiratory movements? But if it be impossible to compensate some of the impediments to respiration without an actual strengthening of the respiratory movements, it directly follows that the success or failure of compensation does not depend alone on the amount of the impediment. This consideration in a great measure explains why a diffuse capillary bronchitis is so much more dangerous to little children than to adults, and also throws light on the fact that extreme pulmonary emphysema or advanced cirrhosis of the organ is so much better, and especially longer, tolerated than a phthisical destruction of the lung of equal or even less extent. The result which, in children at the breast, is due to the imperfect development and the feebleness of the musculature of the thorax, is produced in the phthisical by the atrophy and weakness of the muscles setting in during the course of the disease; in both cases the muscles are incapable of carrying out, for a long time together, vigorous, ample, and deep inspirations. I recently referred to some acute as well as chronic processes which reduce the functional power of the respiratory muscles by injuring their contractile substance; but trichinosis, and progressive muscular atrophy, &c., are incomparably less important, as regards the question now engaging our attention, than is *pyrexia*. For all pyrexial diseases sooner or later depress the energy of the muscles, some of them, like the typhous, to a greater degree than most others. It is this muscular feebleness—which in the phthisical also is in great part traceable to the hectic fever—that constitutes one of the most essential causes of the greater danger to life of diseases of the respiratory apparatus which are accompanied by high and especially by prolonged fever, as compared with equally great but apyrexial impediments to respiration. Lastly, there is another fact which must not be forgotten, one which in cardiac lesions also plays such an important part, namely, the danger lest the muscles which have been overworked for so long a time should finally become *exhausted*. Here too probably, as in the hypertrophied heart, *fatty degeneration* is a consequence or sign of the setting-in of exhaustion. Often enough, however, all fatty degeneration is absent, as well as every macroscopic and microscopic criterion of it, while still the manner in which the muscles act shows only too clearly their diminished functional power.

Yet for the production of stronger respiratory movements it is not enough that the muscles of respiration should be functional and vigorous; they must be stimulated in a corresponding degree, or in other words, the stimuli must be stronger, and *the irritability of the respiratory centre* must therefore be *unimpaired.* The excitation of this centre, owing to the defective gaseous contents of the blood, is of course the cause by which the dyspnœic respiratory movements are initiated; and if, as already mentioned, animals, which are bled profusely or whose blood-supply to the head is cut off by compressing the arteries, breathe dyspnœically, this is simply the reaction of the respiratory centre to the sudden deficiency of oxygen. Abnormal stimulation of the respiratory centre is also the cause of the dyspnœa in many emotional disturbances as well as in the dyspnœic paroxysms of the *hysterical;* and that the extreme acceleration of the respirations due to heat, *i. e.* to *abnormally high temperature* of the blood, is brought about by the direct excitation of the respiratory centre, has, as is well known, been strikingly demonstrated in Fick's laboratory;* lastly, it is much more probable, considering everything, that the dyspnœa of the *uræmic,* which is sometimes so intense, depends rather on the action of the uræmic blood on the respiratory centre than on spasm of the bronchi, as claimed by some writers. But, as will appear without further consideration, the direct inference from these facts is that there will be no strengthening of the respiratory movements *when the excitability of the respiratory centre is diminished.* Is it not only and solely because the latter, like the entire central nervous system, loses its irritability on extreme deprivation of oxygen, that in acute suffocation the period of strongest dyspnœa and of convulsions is followed by the stage of asphyxia, in which the body lies deeply comatose and the strongest stimuli are no longer capable of initiating any respiratory movements? True, in pathology, the complete cessation of irritability of the brain is only possible during the agony; its depression, however, is all the more frequent. In this connection, we have to consider, in the first place, those diseases with which are associated general stupor and impairment of the sensorium, as, for example, typhus fever; in the next place, those processes by which the pressure relations or the regular circulation in the interior of the cranium is disturbed, such as cerebral tumours or hæmorrhage, more especially in the region of the medulla oblongata, and the more extensive inflammations of the pia; but, above all, we have to take into account the extensive group of respiratory lesions, by which the oxygen-contents of the blood are *gradually* diminished. For though only the rapidly progressive impoverishment of the blood in oxygen, advancing to an extreme degree, can quickly destroy the irritability of the medulla, it would be an error to regard the slower and more insidious diminution of the oxygen-contents, though never reaching so high a pitch, as an immaterial change. Rather, just as the functional power of all the organs suffers when, instead of blood abundantly saturated with oxygen, a fluid with more or less impoverished oxygen-contents is conveyed to them by the arteries, so also with the function of the brain, which will the more markedly be impaired, as the integrity and activity of the central nervous system is more dependent on the constant presence of an abundance of oxygen than is the case with other organs.

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* Goldstein, 'Würzburg. med. Verhandl.,' 1871, p. 156; Fick, 'Pflüg. A.,' v, p. 38; v. Mertschinsky, 'Beitrag zur Wärmedyspnoe, I.-D., 1881.

The ways, you see, are many by which the respiratory diseases of one kind or another may, after a brief period or a long one, bring about such an impoverishment of the blood in oxygen as shall be no longer compatible with life, and will accordingly prove fatal. In a number of instances, the impediment to respiration gradually increases in such a way that finally the means of compensation at the command of the organism no longer suffice to overcome it, while in other cases the same result will be produced by the accession of fresh impediments. More frequently, however, it happens that, without any augmentation of the respiratory lesion, the compensation becomes inadequate because the muscles, or nervous system, or both, gradually fail. Lastly, it is not uncommon for the increase of the respiratory impediment to concur with the failure of compensation, which will then, obviously, all the more certainly prove fatal. In all these cases of *slow* *suffocation*, the termination of life is not marked by the same stormy phenomena observed in sudden occlusion of the trachea, in fatal embolism of the pulmonary arteries, or in sudden inundation of the air-passages with liquid. This difference will be rendered intelligible by the slow development of the fatal change in the gaseous contents of the blood, and still more by an accurate consideration of the causes of suffocation, as I have just attempted to expound them to you. For if the respiratory impediment endangers life precisely because the individual concerned is unable, owing to muscular weakness or loss of irritability of the central nervous system, to carry out the dyspnœic respiratory movements necessary to compensation, you cannot properly expect to find this most striking symptom of suffocation in such cases. Call to mind the picture of asphyxia in a curarised animal. If the carotid has been connected with a kymograph, you soon see, on stopping artificial respiration, a considerable rise of the blood-pressure curve, and at the same time the most unmistakable vagus-pulsations; after a minute, or at most a minute and a half, the arterial blood ceases to be distinguishable from the venous; both are very dark, almost black—and in spite of this, you have noticed neither dyspnœic respiratory movements, nor convulsions; indeed not a single muscular twitching has occurred. What is here the result of the paralysis of the motor nerves, is produced in slow suffocation by the muscular feebleness and the deficient irritability of the central nervous system: there is *a complete absence of those striking irritative phenomena*, which in death by acute suffocation precede the asphyxia. There is no extraordinary increase of dyspnœa and no convulsions; similarly the exophthalmos and the dilated pupils are absent, as well as the evidences of irritation of the vaso-motor and vagus centres. Rather, the pulse of such patients is usually small and easily compressible, very frequent and sometimes irregular; the pupils are normal or even contracted, and all the bodily movements feeble and languid. Instead of the cyanosis, which it is easy to see will be more apparent the more full-blooded and vigorous the individual, the face, skin, and visible mucous membranes of such patients take on a bluish grey, dull, almost leaden hue; the temperature is low, and the skin feels cool to the touch. For not only do the movements but all the other functions gradually become paralysed; the patients grow markedly apathetic, or even somnolent, are unaware of all that goes on around them, and unconscious of their own need for air. Hence, in spite of the continuance of a considerable respiratory impediment, the patients neither complain of want of breath nor make increased respiratory movements. They neither sit straight up in bed nor support the trunk with their arms so as to give themselves, or rather their thorax-muscles, a fulcrum for their work; indeed they scarcely make use of the accessory muscles of respiration; their breathing is frequent, but shallow and restricted. Moreover, owing to the defective irritability of the respiratory centre, irregularities in the respiratory movements sometimes develop, and of these none is more interesting than the so-called *Cheyne-Stokes respiratory phenomenon.*

This phenomenon, which was first observed by the Dublin physician Cheyne* and more fully described by Stokes,† consists *in a series of inspirations, increasing to a maximum and then declining in force and length, till a condition of apnœa, a complete respiratory pause, sets in.* This may last so long as to give rise to the impression that the patient is dead, till the pause is terminated by an extremely feeble inspiration. A somewhat stronger inspiration follows, and then others, which, without succeeding one another more rapidly, become deeper and deeper and at last dyspnœic, till finally the patient, groaning loudly, passes into the most extreme degree of dyspnœa. From this moment the dyspnœic character of the respirations grows less and less marked; the breathing becomes gradually shallower till at last it again pauses. The time occupied by these phases may be very unequal: Traube, who paid the closest attention to the entire phenomenon,‡ has observed cases in which four or five such periods (inclusive of the pauses) occurred in one minute, while, in other cases, the pause alone occupied thirty to forty seconds and the duration of the respirations was scarcely less. It is shortly before death and always in severe forms of disease that this remarkable phenomenon makes its appearance. It is not exactly rare; rather it has been observed in various *cerebral diseases*, as tumours, hæmorrhages, basilar meningitis, in uræmic paroxysms, as well as in many *cardiac affections*, as fatty heart, sclerosis of the coronary arteries, imperfectly compensated stenosis of the aorta, &c. It may be experimentally produced by the administration of morphia, as shown by Filehne:* in rabbits the injection 0·05 to 0·1 gram hydrochlorate of morphia into the veins, and in dogs correspondingly larger doses are required, to render the breathing temporarily *periodic*—Filehne's term for the mode of respiration under discussion. However greatly the above-mentioned diseases differ, they have one feature in common, *the reduction of irritability of the respiratory centre* in consequence of the long continued impairment of the arterial circulation of the medulla oblongata; and this is the effect also, which the morphia first exerts on the respiratory centre. To Traube belongs the credit of having first called attention to the importance of this depressed irritability of the respiratory centre in the Cheyne-Stokes phenomenon, although the attempt to base its explanation on this alone was bound to fail. For while, on his assumption, the respiratory pause is quite intelligible, and it is also easy, having regard to the increasingly venous character of the blood during the pause, to understand the period of *increasing* respirations, it is impossible to see why the organism should not thenceforward regulate its breathing, to correspond with the need for oxygen, in the ordinary rhythmical manner, instead of gradually relapsing again into a state of apnœa. To explain this we evidently need some other factor, which Filehne believes he has discovered in the intervention of the innervation of the cerebral arteries. Filehne's line of argument seeks to show that in these cases the gaseous contents of the blood influence the breathing, not only directly by stimulating the respiratory centre, but also indirectly by exciting the vaso-motors of the cerebral arteries; and he assumes that, owing to the diminished irritability of the respiratory centre, the latter effect, and with it the anæmia of the brain, is more promptly initiated than the former. Supposing, then, that for some reason or other a respiratory pause takes place, the consequent deterioration in the gaseous contents of the blood leads first to a contraction of the arteries of the brain and thereby to a gradually increasing anæmia of the medulla oblongata, by which now the sluggish respiratory centre is also stimulated in an increasing degree. By the dyspnœic respirations thus called forth the oxygen-contents of the blood are so augmented that the excitation of the vaso-motor centre passes off, and the respiratory centre is speedily supplied by an abundance of blood which is comparatively rich in oxygen. The irritability of the respiratory centre is, however, too slight to enable it to react to blood of this character by further respiratory movements, and the result is a successive decline of the respirations till they cease completely; whereupon the cycle is repeated. That this is actually the connection of events, Filehne has rendered plausible not merely by theoretical considerations and by accurately determining the blood-pressure in rabbits under the influence of morphia, but by weighty evidence derived from observations at the sick bed. For, on the one hand, he was able to determine that the inhalation of amyl nitrite, if it produced complete paralysis of the vessels, removed the Cheyne-Stokes phenomenon, and found, on the other hand, that little children, displaying the phenomenon, exhibited just before the commencement and during the phase of increasing respirations a distinct depression of the large fontanelle, which cannot properly be referred to anything but a diminution of the blood-supply to the brain. But however attractive Filehne's reasoning may appear, I must not conceal that it has met with more opposition than support from the writers who have since investigated the phenomenon under discussion. In particular, Rosenbach* and Löwit,† who studied the subject in man, as well as Luchsinger and Sokolow,‡ who produced a periodicity in the breathing of a frog by temporarily ligaturing the aorta, have not been able to convince themselves that the alterations in the tension of the vessels take place in the manner described by Filehne.

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* Cheyne, 'Dublin Hospital Rep.,' ii, p. 217.

† Stokes, 'Krank. d. Herzens u. d. Aorta,' trans. by Lindwurm, 1854, p. 267.

‡ Traube, 'Ges. Abhandl.,' ii, p. 882; iii, p. 103.

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* Filehne, 'Berl. klin. Wochenschrift,' 1873, Nos. 13, 14; 'Ueber das Cheyne-Stokes'sche Athmungsphänomen,' Habilitationsschrift, 1874; 'A. f. exper. Pathol.,' x, p. 442; xi, p. 45; 'Zeitsch. f. klin. Med.,' ii, p. 255, 472.

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* Rosenbach, 'Ztsch. f. klin. Med.,' i, p. 583.

† Löwit, 'Prager med. Wochenschr.,' 1880, No. 47.

‡ Luchsinger und Sokolow, 'Pflüg. A.,' xxiii, p. 283.

Owing to its close connection with reduced irritability of the respiratory centre, I have thought it well to consider the Cheyne-Stokes respiratory phenomenon here, although it is met with in diseases which have nothing in common with the respiratory lesions, and does not form a constant, or even frequent, symptom of slow suffocation, in which, at any rate, it is much more rarely observed than any other of the disturbances already described. As to the factor conditioning these disturbances, the actual pernicious agent in these cases of very gradual suffocation, which extend not uncommonly over several days and weeks, on this point no certain information can be given, owing to the want of all analyses of the gases. There is no doubt that in such cases also both alterations are present, *the impoverishment of the blood in oxygen, and the accumulation in it of carbonic acid*; and if in acute asphyxia we had convincing reasons for regarding the want of oxygen as the destructive factor, it is very natural that, owing to the absence of all stormy symptoms and signs of irritation generally, we should here have recourse to a *poisoning by carbonic acid*. Still we were able, as I think adequately, to explain the absence of irritative phenomena by the tardiness of the process, the muscular feebleness, and more especially the reduced irritability of the central nervous system; and you can scarcely entertain a doubt that, for the last of these conditions, the chronic deficiency of oxygen should be made responsible rather than the excess of carbonic acid. We are not as yet in possession of the crucial facts which would enable us to come to an exact decision on the entire question; we neither know to what pitch the loss of oxygen and accumulation of carbonic acid proceed in these cases, nor are we acquainted with the effects of a *chronic* simple deficiency of oxygen or of a permanent excess of carbonic acid; for investigators have hitherto concerned themselves almost exclusively with their acute effects. As regards acute poisoning with carbonic acid, old and more recent experiences agree in teaching that, if slight or moderate in degree, it is attended only by irritative phenomena, in particular by dyspnœic strengthening of the respiratory movements and rise of blood-pressure, while in the severer degrees, such as result from the inhalation of a mixture of gases containing more than 20 per cent. carbonic acid, the irritative phenomena very soon give place to marked *evidences of depression*. The respirations become slower and more superficial, the blood-pressure falls, the movements are languid and sluggish, the temperature is lowered, and the animals fall into a state of stupor, such as would be produced by narcotics, in which they slowly perish, often after the lapse of a considerable time. Although there are many undeniable points of resemblance between this sequence of events and that occurring in slow suffocation in man, we cannot, in my opinion, draw any conclusion whatever from the acute poisoning as regards the latter condition. For that the carbonic acid tension of the blood of the slowly suffocating patient ever attains the values here secured by the experiment is far from clear and *a priori* is very improbable; and on the other hand, it is anything but certain that the irritative phenomena just mentioned persist unaltered, if the slight elevation of carbonic acid tension becomes *permanent*. That analogous considerations apply to the diminution of oxygen-contents I need not again emphasise. Pathological anatomy also leaves us in our difficulty. After the death of a healthy individual from acute asphyxia produced by sudden occlusion of the trachea, the face is extremely cyanotic and an unmistakable venous hyperæmia prevails throughout the whole body; it is rare to miss finding the much-discussed ecchymoses which have been incorrectly attributed by some writers to the rise of arterial pressure exclusively. For this is at most the cause of the small hæmorrhages into the conjunctiva and pia mater, or into other delicate parts in which the capillaries receive no support from the surrounding tissues; but it is not concerned in the production of the much more constant ecchymoses in the parenchyma of the lungs and the pleuræ, since there is no considerable rise of pressure during suffocation in the pulmonary system of vessels. The hæmorrhages occurring under such circumstances in the thorax are due rather to the bad effects exerted upon the blood-vessels and the blood-stream in them by the sudden *rarefaction of the air*, which is necessarily produced by the united influence of the laboured inspirations and the occlusion of the trachea.

They are therefore analogous to the hæmorrhages which follow the application of dry cups and which no one would say were caused by bursting. Now, we have already discussed the cause of the absence of cyanosis in slow suffocation, and if in it there is no abnormal rise of blood-pressure, no rupture of capillaries can occur; still less will you expect, in slow suffocation, to find ecchymoses of the pleuræ, which are the signs of a particular kind of death by acute asphyxia, since the special causes leading to their production are never present in the former. While, then, the absence of all the post-mortem signs characteristic of death by acute asphyxia does not tell against the poverty in oxygen as the determining factor in slow suffocation also, the case in support of the theory of carbonic acid excess is not more favorable. Friedländer and Herter* have noticed, in their oft-mentioned researches, that rabbits and dogs which are made to breathe a mixture of gases containing a large amount of carbonic acid, not uncommonly perish *with the signs of acute pulmonary œdema*, and that in other animals also which succumb to carbonic acid poisoning, hyperæmic and œdematous patches are almost constantly present in the lungs. But any one who would therefore infer that, in those cases of slow suffocation which terminate with œdema of the lungs, or in which the lungs are found to be more or less œdematous post mortem, chronic poisoning by carbonic acid is the cause of all the symptoms, would certainly far overshoot the mark. For, in the first place, the final pulmonary œdema occurs not only, as I formerly stated, in derangements of the respiratory apparatus, but in all varieties of disease, and is nothing more or less than a sign that in the agony the left ventricle of the heart is earlier paralysed than the right; and, again, the writers just named have thrown no light on the mode in which the acute poisoning with carbonic acid brings about the pulmonary œdema, yet this must be known beyond question before one can proceed to draw any conclusion whatever from the appearance or non-appearance of the œdema. Taking everything into account, it seems to me that, in the present state of our science, those who see in slow suffocation the effect of a chronic intoxication with carbonic acid can adduce no better grounds for their belief than can those who look upon the poverty in oxygen as the determining factor not only in acute but in gradual asphyxia.

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* Friedländer und Herter, 'Zeitschr. f. physiol. Chemie,' ii, p. 99; iii, p. 19.

SECTION V.

THE PATHOLOGY OF THE URINARY ORGANS.

WERE we to date the origin of the pathology of the urinary organs from the time when observations were first made on the characters of the urine in disease, we might unquestionably regard this as the oldest and longest cultivated section of our science. For ages before a chemistry of the urine existed, physicians were accustomed to pay the closest attention to their patients' urine, and to attach the greatest importance to its condition as an aid to diagnosis and prognosis. In the medical literature of every century innumerable statements are contained as to the constitution of the urine in the various diseases and in different stages of the same disease—statements which, it is true, have acquired a very different aspect since the most primitive means of examination have given place to the entire physical and chemical apparatus of our laboratories. But although the number of well-founded facts has gradually become so large that a special branch of science has arisen out of them, and with good reason is taught independently, yet the subject-matter of *urinary semeiotics*, as this new discipline might be called, cannot at all be identified with the pathology of the urinary apparatus. In the first place, pathology, like physiology, has to reckon with the fact that the urine does not at once leave the body when produced and immediately become open to investigation; *i. e.* in other words, we have carefully to distinguish between the *secretion* and the *discharge* of the urine. Turning first to the secretion, I need hardly say that a complete theory explaining all the facts does not yet exist. But though we may be painfully sensible of this want, we dare not idly fold our arms, more especially as physiology looks to us for positive guidance and decisive information on many of the questions in dispute. Fortunately we do not need to wait till the normal secretion of urine is elucidated in all its phases; for we already know—and in some respects better than in most other organs—the essential *conditions* on which the physiological secretion depends. We know how intimate are the relations between the renal secretion and the blood—more intimate than in any other gland; for with the blood the kidneys do not simply, like the remaining glands, receive the material out of which they make good their waste and produce their secretion, but there is supplied to them in it all the substances of the urine already formed, so that nothing passes into the urine which was not previously present in the blood, and, on any change in the composition of the blood, there is as a rule an immediate alteration in the composition of the urine. But the urinary secretion, as we have learned mainly through the investigations carried out in Ludwig's laboratory, does not depend merely on the *constitution of the blood*; it is also influenced by the *pressure* and *velocity of the blood-stream*; if the arterial pressure falls below a certain point, the secretion of urine is completely arrested, and—what is perhaps still more decisive—every change of pressure is attended by an alteration in the amount and composition of the urine. It is, further, self-evident that, just as in all other glands, we can count upon a normal renal secretion only when the secretory apparatus, *i. e.* the *glomeruli* and *the epithelium of the tubuli uriniferi*, are intact. Lastly, if the urinary secretion is to proceed regularly *the flow of the urine from the tubules must not be opposed by any abnormal obstacle*. Provided these conditions are fulfilled, the secretion of urine goes on continuously in a regular manner; and, conversely, we may infer that when the secretion is pathological, one at least of these conditions is not met. By these conditions, then, we shall in pathology most advantageously be guided, and it will be our task to examine *how the secretion of urine is affected in morbid conditions of the blood, by abnormal behaviour of the blood-stream, in lesions of the glomeruli and renal epithelium, and in presence of abnormal resistances in the urinary passages.*

CHAPTER I.

INFLUENCE OF THE CONSTITUTION OF THE BLOOD ON THE URINARY SECRETION.

Potential urinary constituents (harnfähige Stoffe).—*The water of the urine.—Salts.—The chlorides of the urine in fever.—Reaction of the urine.—Urea.—Uric acid.—Its origin.—Uric acid infarct of the new-born.—Gout.—Urinary pigments.—Indican.—Sugar.—Biliary constituents.—Hæmoglobinuria.—Periodical hæmoglobinuria.—Fat, spores of hyphomycetæ, and schizomycetes.*

WHILE I just now stated in my introductory remarks that every alteration in the composition of the blood is reflected in the urine, this rule must be qualified to a certain extent if it is to be absolutely correct. For it is fully applicable only to those ingredients of the blood which pass over into the urine, and which may be termed *potential* urinary constituents (*harnfähige Stoffe*). You know of course that normally neither the formed elements of the blood nor the albumen enters the urine, and you will accordingly find it natural that the urine should be uninfluenced by changes in the absolute or relative numerical relations of the blood-corpuscles, and that it should not become albuminous when larger amounts of albumen are supplied to the blood with the food. On the other hand, the number of potential urinary constituents is so great, that our rule loses hardly anything of its importance, in physiology and pathology, through the foregoing limitation. It is owing to the fact that the kidney promptly reacts to every change in the amount of potential urinary constituents contained in the blood that it forms the most effective means of maintaining the composition of this fluid approximately constant, even though the income and expenditure of the organism undergo the greatest variations quantitatively and qualitatively. That the kidney thus acts under pathological conditions also, so that if a patient whose renal function proceeds regularly takes iodide of potassium, it will be excreted in the urine, and that if he drinks more he will, *cæteris paribus*, urinate more, is too obvious to require mention. This being so, it would have little interest for you, were I to enumerate in order all the alterations of the urine thus brought about in disease. For the principle would neither be extended nor placed in a new light by your learning, *e. g.* that in certain diseases the quantity of phosphates contained in the urine is large or small because the phosphates present in the blood are much or little. To explain in this manner all possible individual cases is the office of urinary semeiotics, and we shall do better to confine ourselves to the discussion of such events as are of special practical importance by reason of their frequency, or through which we may at the same time arrive at fruitful conceptions in other directions.

No urinary constituent is so evidently dependent on the blood as that which forms the chief bulk of the urine, and which therefore alone determines the volume or amount of urine secreted; I mean the *water*. For, in the first place, the water is itself an exquisite potential urinary constituent; and, in the second place, we have learned from several researches* of recent years that the excretion of certain substances from the blood is always accompanied by a transudation of water. This is known to be the case with some of the neutral salts which have long been placed among the *diuretics* in our materia medica, *e. g.* nitrate of soda and common salt, and further in a marked degree with urea and urate of soda. From this it follows, evidently, that, *cæteris paribus*, the amount of urine secreted depends on the quantity of water and of these materials present in the blood, of which in a normal condition the urea and the chloride of sodium are most important. In fact, the variations in the amount of urine passed by healthy individuals, though very great, are fully explained by the variations in these particular factors. By partaking of liquids or watery foods the urinary secretion may, as is well known, be increased indefinitely; and, on the other hand, everyone is aware that he who drinks little will urinate little. Moreover, when in midsummer the daily volume is usually relatively small, this is due simply to the fact that large quantities of water are withdrawn from the blood by the very active insensible perspiration, and especially by the abundant secretion of sweat. On the other hand, it is an old experience of the experimental physiologist that a dog produces most urine when it is well fed with flesh and consequently forms a large amount of urea, and that, conversely, when the food is poor in common salt, there is not only less salt in the urine, but less urine is secreted.* If possible still more striking evidence of this connection is afforded by pathology. Thus I may remind you of *diabetes mellitus*, with regard to which we were able to determine that enormous quantities of urine are passed by the patient because correspondingly large amounts of water are consumed; certainly, in comparison with this, the excessive production of urea in the diabetic is of little moment, though it undoubtedly is a factor that increases the amount of urine, which cannot as yet be stated absolutely with regard to the sugar. The most direct contrast to diabetes is presented by *cholera*, in which the voluminous liquid discharges into the intestines cause such a degree of inspissation of the blood and withdraw so much water from it, that the secretion of urine is completely suppressed and absolute *anuria* sets in. This never happens in a physiological condition, even as the result of the most profuse sweating with complete abstention from liquids. Such extreme examples of the influence of the constitution of the blood on the amount of urine are much less frequently observed clinically than are slighter degrees of the same relationship. In severe ptyalism little urine is passed, and the same thing applies, as formerly stated, to the more extreme forms of gastrectasis. This, however, holds generally true of all diseases in which for any reason the patients take little food, though the diminution of the urine is most striking in cases where the nourishment is exclusively or chiefly liquid, as for example, in little children. The constant reduction of the urinary secretion in

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* Heidenhain, 'Pflüg. A.,' ix, p. 1; Grützner, ibid., xi, p. 370; Nussbaum, ibid., xvi, p. 139, xvii, p. 580.

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* Voit, 'Untersuchungen über d. Einfluss d. Kochsalzes, &c., auf den Stoffwechsel,' München, 1860.

fever patients also depends in a great measure on the anorexia, and the consequent small consumption of food, which is not outweighed by the increased thirst of these patients. For although their thirst is considerable as compared with their desire for solid food, yet the absolute amount of liquid taken is probably without exception less than in health, especially in such pyrexial diseases as are accompanied by a dulling of the sensorium. True, in fever we have in addition an increased excretion of water by the lungs, in consequence of the more frequent respirations; an augmented perspiration through the skin, which in all febrile diseases is at least occasionally warmer than normal; and lastly the profuse sweating so frequently setting in in fever patients—all of them factors which withdraw more or less water from the blood, and thus diminish the volume of the urine. But because all these symptoms cease on the disappearance of the fever and the appetite improves considerably, the urine, which was previously scanty and concentrated, usually during convalescence becomes pale and abundant. It may be that, while a pneumonia is undergoing resolution, the water and salts which enter the blood as the infiltration is absorbed may slightly augment the amount of urine secreted; but the chief factor undoubtedly is that after the crisis the convalescent from pneumonia begins to eat and drink with appetite. And if after the puncture of a pleuritic exudation the amount of urine is increased, this is due rather to the increased consumption of food than to the hypothetical augmentation of arterial pressure, whose mechanical basis has besides been rendered doubtful enough by the experiments of Lichtheim (cf. vol. i, p. 105). In these cases the urine is increased because the watery contents of the blood are raised above the normal average value by abundant supplies of water. For on this precisely it depends: only when the normal amount of water is already present in the blood, will the water supplied it at once be excreted in the urine. After an attack of cholera the secretion of urine does not begin with the first glass of water taken by the patient; this does not happen till the blood and the tissues of the body have recovered their normal proportions of water. On the other hand, as regards the effect on the urinary secretion, the source of the abnormal watery contents of the blood is quite immaterial. In winter, when little water is withdrawn from the blood by sweating and insensible perspiration, a healthy person secretes a comparatively large quantity of urine, and the absorption of a dropsical effusion is followed at once by a considerable increase of the urinary secretion. It is especially interesting from this point of view, I think, that anæmic or, more correctly, *hydræmic* individuals should also pass an abundance of urine, which, owing to the amount of water present, is light and at the same time pale—a condition observed by Bauer* to follow even venesection.

The same considerations which apply to the water of the urine hold good of the salts contained in it, of which the chlorides, and chiefly the sodium chloride, make up the great bulk, while the phosphates are of subordinate importance. The greater the amount of salts contained in the blood flowing through the arteries to the kidneys, the more saline matters will be excreted in the urine. The quantity present in the blood depends, however, on the *supply* of salts to it, and on the *amount given up* by it in other directions. For the expenditure in other directions must also be taken into account. The quantity of saline materials *usually* lost in the tears, sputum, and nasal secretion is, it is true, infinitesimal; it is not so, however, in profuse salivation, in severe and extensive catarrh of the bronchi with abundant secretion of mucus, and above all in violent diarrhœa, *e. g.* in cholera. The reason that diarrhœa more especially diminishes so considerably the saline contents of the urine is simply that the absorption of salts—and consequently their supply to the blood—is interfered with; and since the administration of large quantities of salts is followed by diarrhœa, it is not possible to increase the saline contents of the urine above a certain maximum. The salts in question, especially the chloride of sodium, are *per se* very easy of absorption, and provided neither vomiting nor diarrhœa sets in, the salts taken by the mouth can hardly fail to reach the blood. In disease, however, the direct absorption of salts will the more frequently be reduced, because the patients take very little nourishment. This is certainly one of the reasons why in acute *pyrexial* affections the chlorides, and also the phos-

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* Bauer, 'Zeitschr. f. Biologie,' viii, p. 594.

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phates of the urine undergo such a rapid and considerable diminution, so that only minimal quantities are sometimes present; while in convalescence they increase with equal rapidity. But the behaviour of the urinary chlorides in fever is not, I willingly confess, sufficiently explained by this. For their decrease follows so promptly on the commencement of the fever that the amount of nourishment taken cannot possibly be the only determining factor. The cause of the diminution of the urinary chlorides in pyrexial diseases, *e. g.* pneumonia, has been sought further in the storing up of chlorides in the infiltration; but this assumption is at once disproved by the fact that the chlorine-contents of the urine at once begin to increase with the crisis, *i. e.* at a time when the absorption of the infiltration has not yet been properly set going. The inadequacy of these attempted explanations appears most strikingly from the circumstance that fever patients can perfectly well absorb moderate quantities of chlorides introduced with the food, so that not a trace of them can be detected in the fæces, and yet excrete a very small portion in the urine. Röhmann,* who determined this remarkable fact in a number of patients suffering from various acute pyrexial diseases, infers therefrom that the chlorides introduced into the body in fever form with the albumen of the blood-plasma certain combinations which are broken up with difficulty, and consequently interfere with the excretion of chlorine. When, with the fall of temperature, these abnormal combinations become less stable, the excretion of sodium chloride takes place in normal fashion, and is at first excessive in consequence of the antecedent retention.

But just as all the water excreted in the urine does not enter the body as such, but has partly been produced in the organism by the oxidation of substances containing hydrogen, so too the salts of the urine are by no means all exhibited in the same form and amount. Part of the phosphorus contained in the urinary phosphates is derived from the protagon of the brain and nerves, part of the potash from the blood-corpuscles, of the lime from the bones, of the chlorine from the gastric juice, &c. Hence it is not surprising that all the agents which act more or less intensely on the metabolism of the tissues should also affect the excretion in the urine of the salts in question. In this way is to be explained, *e. g.* the comparative richness of the urine of fever patients in potash salts,* the increase of the lime salts of the urine in rapidly growing *cancer of bone*, or other process accompanied by great destruction of osseous substance, and the great decrease in the excretion of lime in extreme, widely disseminated calcification of the arteries.† This relationship is also strikingly manifested in the *reaction* of the urine. It has long been known that the exhibition of soda or potash, as well as of those vegetable salts of the alkalies which are converted into carbonates in the organism, renders the urine alkaline, or at least reduces its acidity; while, conversely, by the administration of phosphoric, sulphuric, hydrochloric, tartaric and other acids, the acid reaction of the urine is increased. Now, normally, a large amount of free acid, not introduced from without, but formed in the organism itself, is constantly absorbed with the gastric juice, and how important this is in its bearing on the acid reaction of the urine is taught in the most objective way by those interesting cases of *gastrectasis*, in which the contents of the stomach are almost wholly evacuated by vomiting, with the result that the urine is constantly *alkaline*.‡ To complete what has been said, as regards the phosphates and sulphates of alkalies also, would not be difficult, yet, in accordance with our plan, we may leave this to special pathology. On the other hand, from the point of view of general principles, it seems worth mentioning that just as the excretion of some salts in the urine influences the water-excretion, so the water-excretion influences the excretion of these salts. Not in so great a degree, it is true; yet the drinking of large quantities of liquids distinctly increases the quantity of salts excreted, so that the dilution of the urine does not exactly keep pace with the increase of volume.

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* Röhmann, 'Zeitschr. f. klin. Med.,' i, p. 513.

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* Salkowski, 'Virch. A.,' liii, p. 209.

† L. Hirschberg, 'Ueber Kalkausscheidung und Verkalkung,' Inaug.-Dissert., Breslau, 1877.

‡ Bence Jones, 'Med.-Chir. Transact.,' vol. xxxv, p. 39, 1852; Quincke, 'Correspondenzbl. f. Schweiz. Aerzte,' 1874, No. 1; Stein, 'D. A. f. klin. Med.,' xviii, p. 207.

Yet it is not only the amount of urine and of saline matters contained in it that is markedly determined by the constitution of the blood supplied to the kidneys, but also the quantity of those bodies which form the final products of the decomposition and transformation of nitrogenous substances, and which are usually termed *specific urinary constituents.* Of these, urea, as you know, plays the principal *rôle* in man, and far exceeds all the others in amount—the uric and hippuric acids, kreatin, &c. Every decomposition of albuminous substances in the organism immediately gives rise to a corresponding amount of urea, which is always rapidly excreted in the urine. The source of the albumen makes no difference. In healthy persons it is pre-eminently the amount and composition of the food that determines the quantity of urea excreted in twenty-four hours; but also in the different diseases nothing more hinders the proper estimation of any irregularities in the excretion of urea than the dissimilarity of the nourishment taken. That a diabetic person occasionally excretes enormous quantities of urea, will surprise no one who has seen the extraordinary amount of flesh consumed by him; and if, conversely, an individual with stricture of the œsophagus secretes a small quantity of urine containing little urea, this is simply the result of the altogether inadequate supply of nourishment. But that the urea may also be derived from the proper constituents of the body is proved by the fact, that when food is completely abstained from, the excretion of urea, though it gradually declines, never ceases completely. As a matter of fact, the decomposition of the proper albumen of the body proves in numerous diseases to be a source of urea, which is all the more abundant the more profuse and rapid the albuminous waste. To this factor alone it is due that the excretion of urea in pyrexia never falls to the low point that would correspond to the nourishment taken; for, as we shall have to consider later, the decomposition of the albumen of the body is abnormally augmented in and by the fever. When dealing with fatty degeneration (vol. ii, p. 671), some other pathological factors were mentioned, which abnormally increase the disintegration of albumen. Here belongs not merely the febrile increase of temperature, but that too which is produced by exposure to an excessively warm surrounding medium; further, *acute phosphorus-poisoning* and certain forms of so-called *icterus gravis*. On the same occasion, I also stated that A. Fränkel has come to the conclusion that everything which diminishes the supply of oxygen to the blood *increases the disintegration of the albumen of the body*, a conclusion to which he was led as the result of his experiments on asphyxia in dogs and on poisoning with carbonic oxide, as well as by Bauer's experience as to the influence of the loss of large quantities of blood on the metabolism. In all these cases he determined the presence of a larger amount of urea in the urine than could be accounted for by the consumption of nitrogenous food. Except the nitrogenous bodies contained in the food and those of the organism itself, no other source of urea exists, and one must always recur to the one or the other when the excretion of this substance is increased. This also undoubtedly holds good of the increased excretion of urea which regularly follows the drinking of large quantities of water and the exhibition of chloride of sodium and other diuretic salts. At any rate, by far the most plausible explanation of this fact, first determined with accuracy by Voit,* is, that the more abundant juice-stream bathing the tissues of the body carries off with it larger quantities of albumen and thus causes its decomposition. I was fully justified, you see, in placing the dependence of the excretion of urea on the constitution of the blood side by side with that of the water and the salts; indeed in one respect the case of urea is simpler, as there is hardly ever a necessity to take into account its excretion by any organ except the kidney. For though urea, owing to its great diffusibility, may pass over into the lymph and transudations, and even into the saliva, gastric juice, succus entericus, and probably other secretions also, yet provided the function of the kidneys be regular—and we assume this in our present discussion—the quantity entering these fluids is so small that, as compared with the amount excreted by the kidneys, it may safely be altogether neglected. Violent diarrhœa must, it is true, diminish the urea-contents of the urine, not because much urea is then excreted from the intestine, but because it must hinder the absorption of the albumens of the food. For the rest, one might naturally refer here to the large accumulations of serous and dropsical fluid, in which urea is invariably present, it may be in tolerable abundance.[*] Edlefsen[†] has found, in fact, that the absorption of a general dropsy is attended by a gradual but considerable increase of urea in the urine, in the production of which result the augmentation of the juice-stream as well as the improved appetite may have a share.

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* Voit, 'Untersuchungen über d. Einfluss d. Kochsalzes, &c., auf den Stoffwechsel,' München, 1860.

Matters are much less clear in the case of *uric acid.* True, there is no doubt that uric acid is also a body derived by oxidation from material originally albuminous, and that this material may equally well be albumen of the food or of the organism itself. Hence the excretion of uric acid is increased by an abundant diet, especially one consisting of flesh, and decreases on fasting, although the much smaller absolute amount of uric acid excretion makes it impossible that its variations should at all be comparable to those in the production of urea. But even so, the bare fact that uric acid is one of the final products in the retrogressive metamorphosis of the albuminous bodies is not of much avail, so long as we know so little of its actual mode of formation, and especially while we are so completely uninformed as to its relations to urea. Its chemical composition suggests the idea that it forms a direct antecedent stage in the production of urea, and the experiments of Frerichs and Wöhler,[‡] according to which the exhibition of uric acid causes an augmented excretion, not of this body, but of urea, appear to afford strong confirmation of this view. Still Salkowski,[§] who recently repeated these experiments, could not feel certain of the correctness of their results; rather it appeared to him highly probable that from uric acid *allantoin* is formed—which, it is true, according to its composition, appears to be an antecedent of urea. But even if it were certain that the organism has the power of breaking up the uric acid taken into urea and oxalic acid, or, on complete oxidation, into urea and carbonic acid, it is far from thereby proved that the uric acid actually excreted from the body is proteid material which had *not yet* been oxidised into urea. Rather, such a supposition appears to me to be scarcely compatible with the fact that in healthy individuals, even with the greatest variations in the consumption of albuminous food and the greatest differences as regards physical exertion and other habits, the mutual relations between the excretion of uric acid and urea always remain approximately the same. As for the support which the assumption has been supposed to receive from pathology, this also is weak. Bartels, in his well-known investigation,* has attempted to prove, on evidence derived from systematic analysis of the urine, that in all diseases attended by considerable respiratory disturbance the excretion of uric acid increases, the mutual relations between uric acid and urea being altered to the disadvantage of the latter. Yet this view has not been confirmed by later investigations, and Senator† also has only occasionally seen an increased excretion of uric acid in artificial disturbance of the respiration, while in the great majority of cases this excretion remained unaltered. Even with regard to the *uric acid infarcts* of the new-born and the abundant production of uric acid during the first few days of life, the obstetricians‡ who assume that the albuminates taken in large amount are *not yet completely* oxidised, would find it difficult to produce proofs of this. Certainly inadequate supply of oxygen to the blood cannot be made responsible for the "incomplete combustion," since, according to my experience at least, the uric acid infarcts are found in strong children who have breathed admirably, while I have most often failed to discover them where extensive atelectases or bronchitis and broncho-pneumonia were evidence that the child's respiration was defective. Such being the position of affairs, it is useless to refer the increased excretion of uric acid, so often observed§ in the *leukæmic*, to an impoverishment of the blood in oxygen, the more so because all leukæmic patients do not suffer from dyspnœa. Moreover, Pettenkofer and Voit[*] could detect no abnormality in the absorption of oxygen and excretion of carbonic acid in a leukæmic person, whose uric acid excretion was increased by 64 per cent. Whether, indeed, the other hypothesis,[†] which attempts to find the reason of the increased excretion of uric acid in the augmented supply of this substance from the hypertrophic organs, especially from the spleen, more nearly approaches the truth, cannot be decided at present; the fact that there is not an increased excretion of uric acid in all splenic enlargements does not so strongly tell against the theory as was supposed by Bartels.

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[*] Naunyn, 'A. f. Anat. u. Physiol.,' 1865, p. 166.

[†] Edlefsen, 'Med. Centralbl.,' 1878, p. 513.

[‡] Frerichs u. Wöhler, 'Annal. d. Chemie und Pharm.,' lxv, p. 335. Also Zabelin, ibid., 1863, Supplemt., ii, p. 326

[§] Salkowski, 'Ber. d. deutsch. chem. Gesell

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* Bartels, 'D. A. f. klin. Med.,' i, p. 13.

† Senator, 'Virch. A.,' xlii, p. 1.

‡ Cf. Spiegelberg, 'Lehrbuch der Geburtshülfe,' 1878, p. 228.

§ Salkowski, 'Virch. A.,' l, p. 174, contains quotations from several other authors, lii, p. 58.

Nowhere does our want of acquaintance with the history of the origin of uric acid, and with the conditions under which part of the albuminates are oxidised into this substance, make itself so seriously felt as in *gout*. For ages, as is well known, a luxurious and free manner of life, immoderate eating and drinking, and especially an excessive animal diet with an inadequate amount of exercise, have been made responsible for the production of gout; and since, about the beginning of this century, it became known that uric acid forms the chief constituent of the gouty deposits, and that the blood of the gouty is abnormally rich in this body, the theory was soon started that incomplete oxidation of the albuminates taken in excess is the cause of the increased production of uric acid. The theory has been repeated by one writer after another up to the present day, although its weak points are apparent enough. In the first place, it neglects those cases where persons who notoriously have never in their lives indulged in any kind of excess, suffer from the most severe paroxysms of gout. Every busy practitioner is acquainted with such cases, and we, pathological anatomists, have from year to year opportunities, even in this part of the country where gout is not very frequent, of examining the bodies of persons who, though they lived in the most needy circumstances, have a more or less large number of joints abundantly incrusted with most typical urates. On the other hand, who does not number amongst his acquaintances persons who are accustomed daily to indulge to excess in food, especially such as is rich in albuminates and fats, who put no restraint on their indulgence in strong wines, who avoid as far as possible all physical exertion, and yet, though all the supposititious causes concur in their case, have never had even the slightest indication of podagra? And then *heredity*, which in few diseases plays such a part as here, and to which it is due that even children have, though only exceptionally, their regular paroxysms; is one to attribute the gout in these boys to gluttonous habits and want of exercise? Naturally, it does not occur to me to question the fact that the uric acid of the gouty is derived from the albuminates; but the production of that amount of the substance with which we have to deal in gout—a contents of 0·05 per thousand, of the serum is high—does not in truth demand a very large supply. This is not the real difficulty; but the crucial question is—How does it happen that in the gouty the uric acid and urea are not produced from the albuminates in the same quantitative proportions as in health? To this question we are at present unable to give anything approaching a satisfactory answer; for the want of exercise and the reduced supply of oxygen depending upon it are mere arbitrary assumptions, the unsubstantial character of which I have just attempted to show. Taking everything into account, I hold it to be not certainly made out that the excessive supply of albuminates has any essential influence on the production of uric acid: the most I can concede is that *in the gouty* much uric acid is produced in consequence of this mode of diet; a non-gouty person would produce a large amount of urea if his manner of living were the same.

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[*] Pettenkofer und Voit, ‘Zeitschr. f. Biol.,’ v, p. 320.

[†] Virchow, his ‘Archiv,’ v, p. 108; Ranke, ‘Be [illegible] und Versuche über d. Ausscheidung der Harnsäure beim Mens [illegible] 28.

But even were we acquainted with the origin of uric acid in the gouty, we should not have gained much. For we should still have to explain why this uric acid is not excreted in a normal manner by the kidneys instead of into other localities, namely *the joints*. Bearing in mind the continuously increased excretion of uric acid in the leukæmic, it cannot be asserted that the kidneys are unable to excrete more than a certain amount of this substance; moreover, the deposition of urates in the joints occurs only temporarily, during the paroxysms, so long as the typical character and course of the affection are adhered to. Garrod,* whose investigations into gout may still be regarded as the most thorough and careful that have yet been made, was induced by this very fact to attribute the paroxysms to *derangements of the renal function.* In this view he was greatly strengthened by the evidence first brought forward by himself, and since then often confirmed, that just before, and certainly during, the attack the uric acid contents of the urine are *abnormally small,* being reduced even to less than half the usual amount. The quantity of urine secreted, the amount of urea, of alkalies and of alkaline earths as well as of phosphoric acid are also reduced, at least during the first few days of the paroxysm, as has repeatedly been determined by careful observers. Still any one who has seen an unfortunate patient in the first few days of the attack, during which the suffering is most acute, will not be greatly surprised at his secreting urine which is poorer in urea and salts than that of a healthy person; nor is there, in my opinion, the least ground for believing that the falling off in uric acid is due to a disturbance of the secretory activity of the kidney. For that the kidneys are invariably and from the start diseased in the gouty is a perfectly arbitrary assumption; on the contrary, the urine continues to be for years absolutely normal in the intervals between the attacks. How if the reverse were true,—that so little uric acid is excreted by the kidneys because a certain quantity has been deposited in one or other of the joints? Our main difficulty in arriving at a decision has always been the complete dearth of *quantitative* evidence. How quick has been the disposition to rely on the fact that ligature of the ureters in birds and snakes is rapidly followed by an abundant deposition of urates in the body!† Yet, to say nothing of the circumstance that these deposits are far from being confined exclusively to the joints, but occur just as early and abundantly in the serous membranes, the lungs, and some other localities, which never become the seat of gouty deposits in man,—independently of this, I say, uric acid takes the place, in the classes of animals just named, of the urea in mammals, and it need excite no surprise that when its excretion is prevented it should accumulate to such an extent in the body that the salt, which is with difficulty soluble, can no longer be kept in solution by the juices. A mammal, on the other hand, after ligature of the ureters, never exhibits a deposit of urates in any locality, even when it survives the operation for five or six days or more, and whether it is possible for a gouty person, as the result of a diminution in the excretion of uric acid extending over some days, to accumulate such a quantity of urates in the blood or the juices of the parenchyma that the latter are unable to keep them in solution is accordingly more than doubtful.

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* Garrod, 'The Nature and Treatment of Gout and Rheumatic Gout,' London, 1859. Trans. by Eisenmann, Würzburg, 1861, pp. [illegible]-212.

† Zalesky, 'Untersuchungen über d. uräm. Process [illegible] der Nieren,' Tübingen, 1865.

An hypothesis, which was also formulated by Garrod, and has recently been more thoroughly worked out by Senator,* appears to me to be more plausible, and is at any rate worth noticing. According to it, the precipitation is not due to an excessive accumulation of uric acid in the blood, but to *a decrease in the power*, possessed by the blood and lymph, *of keeping it in solution*. Senator reminds us that the urine very frequently throws down a sediment of urates, without any increase of its uric acid contents, when its acid reaction is unusually strong; and he thinks that, owing to some digestive disturbance or other, organic acids, such as lactic and volatile fatty acids, arise, which, on passing into the blood, may reduce its alkalinity. That in gout the blood and lymph are less alkaline than in health has not, it is true, been so far determined; still there can be no mistake as to the striking utility of the regular use of alkaline waters, especially those of Karlsbad, in most cases of gout, which would favour the above hypothesis; and the conspicuous muscular feebleness, of which the gouty complain during the paroxysm, at any rate does not tell against it. But why the deposition of the urates should take place precisely in the *joints*, and should display such an extraordinary preference for the *metatarso-phalangeal joint of the great toe*, this we must honestly confess is beyond our comprehension. We are ignorant whether cartilaginous tissue is related in any way to the production of uric acid or whether it possesses the power of attracting the urates; and while Hueter* lays stress on the fact that this same joint is also frequently attacked in simple panarthritis, this tends the less to throw light on the subject of podagra, as there are numbers of gouty persons who for many years pass through their regular attack in the spring, but whose joints are perfectly sound and normal. Instead of being satisfied with this and similar mere phraseology, we shall do better, I think, to confess openly that not the least difficult problem in this enigmatical disease is the question of its localisation.

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* Garrod, loc. cit., 215; Senator, in Ziemssen's 'Handb.,' xiii, Abtheilg. 1.

While we shall pass over the remaining specific urinary constituents which are counted among the final products of the metamorphosis of the albuminates, we may spend a moment in considering the *pigments* of the urine. Since, so far as we know, the kidneys have no share in the production of urinary pigments, their excretion is altogether dependent, qualitatively and quantitatively, on the constitution of the blood supplied to these organs, *i. e.* on the nature and amount of pigment contained in the blood. The chief pigment of normal urine, Jaffé's urobilin,† is, as shown by Hoppe-Seyler,‡ in the last instance a derivative of the colouring-matter of the blood, and the amount of urobilin excreted in a certain period is therefore determined by the quantity of red blood-corpuscles disintegrating during the same interval. This is the explanation of the fact that the urine in pyrexia is not only, as we have seen, rich in potash salts, but abounds in pigment; a condition which must not be confounded with the bright red colour of this urine. For the red colour implies simply that in that particular portion a *relatively* large quantity of pigment is contained, but does not give any grounds for concluding as to the *absolute* quantity excreted in twenty-four hours; in fever the urine must be bright red because it is scanty, and in polyuria the urine is always pale. But it is not only the normal urinary pigments, but the pathological also, that are conveyed to the kidneys with the arterial blood, although we are not always able to certainly state their source. The origin of two brown or red pigments, which Baumstark[*] prepared from the deep brown urine of a leper, should be referred, according to him, to a diseased condition of the spleen. If, further, the urine of persons having melanotic tumours not uncommonly contains a peculiar *chromogen*, which lends the urine an intensely dark hue on oxidation, by exposure to the air, after treatment with chromic acid, &c., it is natural to suppose that this chromogen is derived from the melanoses. As regards *indican*, I formerly stated (vol. iii, p. 977) that the amount contained in the urine is larger, the more the indol produced by intestinal putrefaction becomes absorbed, and that it consequently is present in large amount more especially in intestinal stenoses involving the ileum. But though the mode of origin of the indican is here apparent enough, this cannot be asserted of many other cases in which the urine is rich in this body.[†] In some cases of diffuse peritonitis without intestinal obstruction, Jaffé[‡] found an enormous amount of indican in the urine; Senator[§] found an increased indican excretion, more or less great, in very different diseases; above all in chronic wasting and consumptive diseases, more especially in cancer of the stomach, in advanced pulmonary phthisis and tabes mesenterica of children, in morbus Addisonii, in lymphosarcomatosis, &c. But the circumstances which in these diseases give the blood its richness in indican, elude, as has been said, all explanation.

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* Hueter, 'Klinik d. Gelenkkrankheiten,' 1871, p. 348.

† Jaffé, 'Med. Centralbl.,' 1868, p. 241; 'Virch. A.,' xlvii, p. 405.

‡ Hoppe-Seyler, 'Ber. der deutsch. chem. Gesellsch.,' vii, p. 1065.

The excretion of *sugar* with the urine was thoroughly discussed in connection with the pathology of the liver and diabetes, so that I need hardly repeat that it depends only and solely on the sugar-contents of the blood. Because normal blood contains only a very trifling amount of sugar there is very little present in normal urine, and since in healthy individuals the sugar-contents of the blood is not increased by the consumption of carbohydrates, the amount of sugar in the urine is also not augmented. Any one, however, in whom the blood becomes glycæmic, either constantly or after the consumption of carbohydrates, at once begins to pass urine containing sugar, and consequently becomes *diabetic*. On the same occasion we discussed the very different circumstances under which a transitory glycæmia and glycosuria may arise. It will therefore be sufficient to point out here that, while in ordinary glycæmia and glycosuria we have always to deal with grape-sugar, other kinds which are not altered in the blood may pass over into the urine. The *inosite* which is excreted with the urine is also conveyed to the kidneys by the blood, and the sugar appearing in the urine of lying-in women in consequence of the retention of the lacteal secretion has been shown by Hofmeister* to be *sugar of milk*.

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[*] Baumstark, 'Pflüg. A.,' ix, p. 568.

[†] Eiselt, 'Prager Vierteljahrschr.,' Bd. lxx and lxxvi; Pribram, ibid., lxxxviii, p. 16; Ganghofer und Pribram, ibid., cxxx, p. 77.

[‡] Jaffé, 'Virch. A.,' lxx, p. 72.

[§] Senator, 'Med. Centrlbl.,' 1877, Nos. 20, 21, 22. Cf. also Hennige ('D. A. f. klin. Med.,' xxiii, p. 271), who observed the increase of the indican contents of the urine chiefly in general disturbances of nutrition, depending on disease of the digestive canal; further, Heinemann ('Arch. of Med.,' 1880, Aug.), who found the greatest increase in malignant tumours of the abdomen.

Still more striking, if possible, than in the case of the substances already discussed is the influence of the constitution of the blood on the urine *with regard to those bodies which are not usually contained in it*. If, as is well known, innumerable substances which have somehow entered the organism are excreted with the urine, this evidently implies simply that owing to the altered composition of the blood the composition of the urine is also altered. You will not expect me to enumerate all the organic and inorganic substances which reach the urine in this way, and are there occasionally detected, more especially as most of those substances which are introduced from without and enter the urine have no essential pathological interest. True, the attention of pathologists has long been excited by the fact that, in spite of the healthiness of the kidneys, heterogeneous constituents may appear in the urine, which are undoubtedly products of the organism itself. Besides the sugar just mentioned, I refer chiefly to the *constituents of the bile*. That bile-pigments and bile-acids may appear in the urine when the bile is kept from entering the intestine, and is afterwards absorbed, has been dwelt on with sufficient minuteness when dealing with the pathology of

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* Hofmeister, 'Zeitschrift f. physiol. Chemie,' i, p. 101.

icterus; and on a previous occasion (vol. i, p. 476) I informed you that if small amounts of free hæmoglobin circulate in the blood they may be converted under certain circumstances into bile-pigment, and in this form be excreted with the urine. But even albuminous bodies may appear in the urine secreted by perfectly healthy kidneys, simply when and because they are contained in the blood. This is, perhaps, less remarkable with regard to *peptone*, which, in fact, if directly injected into the blood or subcutaneous cellular tissue, at once makes its appearance in the urine. And since, as I formerly mentioned (vol. i, p. 328), peptone has been repeatedly detected in pus and in the products of fibrinous inflammation, it is not surprising that Hofmeister[*] and his pupils were able to discover it in the urine of patients during the absorption of pneumonic and pleuritic exudations, in purulent effusions, in rheumatism of the joints, &c. Certain albuminous bodies coagulable by heat may also pass directly from the blood into the urine. Thus it has long been known that dissolved egg-albumen gives rise to albuminuria when injected directly into a vein or beneath the skin, and that the albuminuria lasts at least till all the egg-albumen has been removed from the body.[†] Similarly, Runeberg[‡] found that the albuminous substance, which he procured by precipitating caseine with acetic acid, and then dissolving in water containing some soda, had passed in about an hour after being introduced into the veins into the urine. Whether, as Runeberg believes, the passage into the urine of the albuminous bodies just referred to depends on *their ready filtration* is doubtful, since the differences in this respect between the various albumens, *e. g.* egg-albumen and serum-albumen, are not so very considerable. Possibly the factors, shortly to be discussed, by which the physiological urine is kept free from albumen are powerless when opposed to those peculiar albuminous bodies, or it is possible that the presence of the latter in the blood is itself sufficient to render the factors ineffectual; but however this may be, the fact remains that those albumens easily and rapidly pass from the circulating blood to the urine. While in this instance we have to deal with materials which do not, in the natural course of things, occur in the human organism, there exists another substance, which, though very different in other respects, shares with them the power of passing into the urine, and is found in large quantities in the body. I mean *hæmoglobin*. In fact, *hæmoglobinuria* forms an equally striking and important symptom in various pathological conditions. It is obvious that an appearance so conspicuous as the *dark- to black-red colour of the urine* could not escape the observation of the older physicians also; yet such cases were long confounded with those in which blood is mingled with the urine. But though the power to distinguish *hæmoglobinuria* from *hæmaturia*, *i. e.* the admixture of blood-corpuscles with the urine, is an acquisition of the last decade, we have already become acquainted with an entire series of pathological processes in which hæmoglobinuria forms a constant symptom. The elucidation of this question in so comparatively short a time is due solely to pathological experiment, which may indeed be said to have formed the starting-point of our knowledge of this subject. By experiment it was discovered that when a moderate quantity of hæmoglobin is set free in the blood-serum, hæmoglobinuria follows. This certainly occurs when a considerable number of blood-corpuscles are dissolved in a short time; indeed, their solution is not necessary; the separation of the hæmoglobin from the stroma of the corpuscles suffices. This may be brought about in various ways, *e. g.* by the introduction of large quantities of *distilled water* or of salt solution of such percentage contents as is not indifferent for the blood-corpuscles of the species of animal concerned; further, by the injection of *cholates* into the blood, or of diluted *glycerine* beneath the skin, &c. After any of these procedures the urine becomes more or less deep red, and shows in the spectroscope *the bands of oxyhæmoglobin, though it contains no blood-corpuscles.* When, further, this condition of the urine had been occasionally observed in human pathology also, as after poisoning with *arseniuretted hydrogen*[*] and with *hydrochloric acid*,[†] it began to be noticed more frequently, as I formerly stated (vol. i, p. 439), at the time when *transfusions of lambs' blood* were undertaken. It is also a very common symptom in extensive *burns*, which do not prove rapidly fatal; and recently hæmoglobinuria has been described by Marchand[‡] as the effect of poisoning by *chlorates*; by Neisser after poisoning by *pyrogallic acid*[§] applied externally, as well as by naphthol;[||] by Boström in consequence of poisoning by *mushrooms*.[¶] All the instances last mentioned in which urine containing hæmoglobin is observed at the bedside, though very different in character, agree in this, that considerable quantities of hæmoglobin are set free in a short time. The poisons just named, if present in certain concentration, have the effect of dissolving and disintegrating the red blood-corpuscles; and you also know that the blood-corpuscles of one species are, as a rule, rapidly destroyed in the blood of another, while, as regards burns, the excessive heat applied to the injured portions of the skin during the infliction of the burns exerts a destructive effect on the blood-corpuscles which are meanwhile passing through the vessels of these parts.[**] Hence the condition of the urine, which is almost always scanty, is very similar in all these cases. In mild cases the urine acquires a more or less deep red colour through the dissolved hæmoglobin, while formed elements may be quite absent from it; in more severe ones the process is not thus restricted, for the urine deposits a brown-red sediment that contains, besides all sorts of molecular detritus, *highly peculiar formed constituents*. At first sight these remind one, in colour and form, of clumps of red blood-corpuscles, but only when hastily looked at. For not only is the colour of the structures contained in the sediment a more intense yellow, and their resistance to reagents greater, than that of true red blood-corpuscles, but one quickly perceives that what at first appeared to be blood-discs are really *globular drops of very unequal size,* which are here and there arranged like strings of pearls and are often confluent with one another. These remarkable structures, compared by some to drops of gum, most closely resemble, I think, in their whole configuration the so-called myelin-drops, which are so prone to form from the medullary sheath during the preparation of nerves; they are not merely met with in the urine, but in fatal cases are usually present in the kidneys, where a much better opportunity of studying them is afforded. Here they are most abundant in the interior of the straight urinary tubules, but are also found, at least when the hæmoglobinuria has continued active till death, in the convoluted tubules and interior of Bowman's capsules,* and it is the presence of these coloured masses that chiefly gives the kidney that dark brown-red hue which was regarded by older observers as simply the expression of marked hyperæmia. These kidneys are usually hyperæmic, it is true, but the really characteristic feature, the *dark brown radiating markings,* corresponding in direction to the straight tubules, have nothing to do with over-fulness of the vessels. Now, the meaning of these yellowish-red masses I need not explain to you; *they consist of nothing but hæmoglobin.* Whether the appearance is due to a precipitation of the hæmoglobin after it has entered the tubules in solution, or whether the passage of the hæmoglobin into the lumen of the latter takes place in the characteristic form of drops, we are so far ignorant; but at any rate it indicates that a large quantity of blood-pigment is excreted with the urine. This alone suffices to explain why it is that cases in which the excretion of hæmoglobin takes place in somewhat consistent masses always run a severe course, and it consequently appears to me to be doubtful whether the plugging of the uriniferous tubules by the hæmoglobin is really so important as Ponfick and others are inclined to assume. For while it is quite true that the confluent and compressed hæmoglobin-drops may block the tubules just as do casts, it is hard to see why they should not be washed away with the urine, just as happens with ordinary albuminous casts. That this *may* occur is proved, moreover, by an examination of the urine passed; and if, when the affection has progressed, hæmoglobin casts cease to be washed away *sub finem vitæ*, this in all likelihood is due mainly to the very comprehensible fact that the urinary secretion of the individual, seriously diseased as he is, gradually ceases as death approaches.

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[*] Hofmeister, 'Ztschr. f. physiol. Chemie,' iv, p. 253; Maixner, 'Med. Centralb.,' 1879, p. 593, 'Prager Vierteljahrsschrift,' cxliii, p. 78, 1879; Jacksch, 'Prag. med. Wochensch.,' 1881, Nos. 7 to 9.

[†] Stokvis, 'Récherches expér. sur l. conditions pathologiques de l'albuminurie,' Bruxelles, 1867, also 'Journ. de méd. de Bruxelles,' vol. xlv; Lehmann, 'Virch. A.,' xxx, p. 593; A. Kuipers, 'Ueber d. Veränderungen in d. Nieren u. d. Harnsecretion nach Injectionen von Hühnereiweiss,' I.-D., Amsterdam, 1880.

[‡] Runeberg, 'D. A. f. klin. Med.,' xxiii, p. 41, 225.

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[*] Wächter, 'Vierteljahrsschr. f. gerichtl. Med.,' Bd. xxviii.

[†] Naunyn, 'A. f. Anat. und Physiol.,' 1868, p. 401.

[‡] Marchand, 'Virch. A.,' lxxvii, p. 455.

[§] Neisser, 'Zeitschr. f. klin. Med.,' i, Heft 1.

[||] Neisser, 'Med. Centralbl.,' 1881, p. 545.

[¶] Boström, 'Sitzungsb. der Erlang. phys.-med. Gesellsch.,' June 14, 1880.

[**] Cf. v. Lesser, 'Virch. A.,' lxxix, p. 248, contains references to the literature.

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* H. Bridges Adams, 'Hämoglobinausscheidung in d. Niere,' I.-D., Leipsig, 1880.

If, accordingly, under these various circumstances, the hæmoglobinuria is not a symptom or effect of renal disease, but the result of a profound blood-change, it is natural to assume a like alteration in those cases also where *marked hæmoglobinuria appears* in a measure *spontaneously*, or at any rate in the absence of any of the above-named or similar causes. This remarkable symptom has often been seen in the course of severe general affections accompanied by pyrexia; thus Immermann has observed it in typhoid and Heubner in scarlet fever;* and for these cases precisely we need hardly hesitate to assume that, under the influence of the disease, a great destruction of red blood-corpuscles has occurred in a short time,—that, if you will, a true *blood-dissolution* has taken place. This is, certainly, in these diseases a rare event, yet the unusual feature is simply the *rapid* and *great* destruction of the blood-corpuscles, for no one doubts that, in the pyrexial infective diseases, conditions are presented which abnormally increase more or less the disintegration of blood-corpuscles. Evidence of this is afforded even in cases of slight or moderate intensity by the increase of the urinary pigment and salts of potash; and when, during the course of the more severe cases, an icteric hue of the skin and urine is not uncommonly noticed, this is but an indication that the destruction of the blood-corpuscles has undergone a considerable increase. Nevertheless, it remains within such bounds that it is still possible for the organism to secure the conversion of the free blood-pigment into bile-pigment—a task to which it ceases to be equal, only when the amount of hæmoglobin entering the blood-serum in a short time is too great.

It is otherwise, however, with the *periodical or paroxysmal*

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* Immermann, 'D. A. f. klin. Med.,' xii, p. 502; Heubner, ibid., xxiii, p. 288.

hæmoglobinuria, which has recently given rise to so much discussion.* For here we have to deal with individuals who appear to be perfectly healthy, and in whom the sole irregularity is the appearance of short attacks of hæmoglobinuria. In the milder degrees the patients complain only of a certain chilliness, and their well-being is not essentially disturbed; the more severe attacks, on the contrary, are ushered in by intense rigors, lasting half an hour or more, which are followed by heat and sweating, and during this time and subsequently the patients feel shattered, extremely languid, and depressed. But the characteristic symptom is the passage after the rigors—during them the urinary secretion is arrested—of urine which is *a dark red solution of hæmoglobin.* Each following portion becomes clearer, and usually during the next twelve to twenty-four hours the subjective troubles, and with them the hæmoglobin-contents of the urine, disappear. The paroxysms vary not only in violence but in frequency. In one point, however, almost all observers agree, namely, that the individual attacks are induced by *lowering of the temperature of the skin, i. e.* by an actual *chill.* The affected individuals are usually attacked only in winter, and then only on leaving their warm houses; and should anyone still doubt this connection he ought to be convinced by Rosenbach's† bold experiment—remarkable owing to its positive success—in which a typical attack was called forth in a patient with paroxysmal hæmoglobinuria by means of a cold foot-bath. Paroxysmal hæmoglobinuria is only very exceptionally observed without antecedent reduction of the temperature of the skin, as in Fleischer's case,‡ where a strong soldier got dark red urine after every somewhat rapid and long march. If it be asked how this periodical hæmoglobinuria should be explained, I reply that here, too, renal disease may, I think, for convincing reasons be excluded. For the hæmoglobin-contents form the only abnormality of this urine; in typical cases the urine is perfectly clear, without any pathological sediment or formed elements, nor besides hæmoglobin does it contain anything, in particular any serum-albumen. In a case examined by Roux with reference to this point in our laboratory, there was iron enough present to admit of the entire amount of albumen being calculated as hæmoglobin. But if in isolated cases a few hyaline or brown casts have been found in the urine passed during a paroxysm, this does not justify the assumption of renal disease, since the casts may equally well have originated from the hæmoglobin in the tubuli uriniferi; and certainly their presence cannot weigh at all against the fact that in the vast majority of all cases *the urine is perfectly normal in the intervals between the attacks*, both immediately before and after the paroxysms. We are accordingly led *per exclusionem* to the hypothesis that paroxysmal hæmoglobinuria also depends on a rapid destruction of large numbers of red corpuscles in the circulating blood; and this probability is raised to a certainty by the evidence obtained by Kuessner,* who proved in a patient so affected that *the serum of the blood obtained during the paroxysms* by cupping *is ruby-red* in colour, while in the intervals it is of the usual bright yellowish hue. Moreover, the notorious and unquestionable connection of the paroxysm with a chill of the skin suggests the idea that all or part of the blood-corpuscles of the affected individuals are *abnormally sensitive to moderate degrees of cold;* and Ehrlich† has in fact succeeded in proving the correctness of this hypothesis by means of a simple and ingenious device. In a woman, aged twenty-seven, who suffered from typical hæmoglobinuria *ex frigore*, and in whom a specimen of blood taken in the usual way during the paroxysm showed nothing abnormal, he succeeded in demonstrating an extensive solution of the red blood-corpuscles in a drop of blood obtained from the finger after it had been bound round with an elastic bandage, and placed first for a quarter of an hour in ice-cold water and then in lukewarm water for an equal period; while in healthy individuals there is no change in the blood as the result of this procedure, there were here, besides many perfectly normal red corpuscles, a very large number of *poikilocytes* and *microcytes*, and in particular a multitude of *stromata undergoing decoloration* or already *completely deprived of colour.* It is on these latter that Erhlich lays chief stress, because their presence is calculated to explain the hæmoglobin-contents of the serum, and hence the hæmoglobinuria, which, on the other hand, is very far from a usual accompaniment of the micro- and poikilocytes when occurring alone. To what process these blood-corpuscles, which are so unduly susceptible to cold, owe their origin, is, it is true, quite unknown at present.

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* Cf. Lichtheim, 'Volkm. Vortr.,' No. 134, contains numerous references to the literature; A. Murri, 'Della emoglobinuria de freddo,' Bologna, 1880.

† Rosenbach, 'Berl. klin. Wochenschr.,' 1880, No. 10.

‡ Fleischer, 'Berl. klin. Wochenschr.,' 1881, No. 47.

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* Kuessner, 'D. med. Wochenschr.,' 1879, No. 37.

† Ehrlich, 'D. med. Wochenschr.,' 1881, No. 16.

We may take this opportunity of pointing out in passing that the symptom of hæmoglobinuria has considerable importance not only from the positive but from the negative side. For if hæmoglobinuria sets in regularly when a large number of red corpuscles has perished in a short time, it is fair to conclude from its absence that no such blood-dissolution has taken place. From this point of view, *the complete dearth of hæmoglobin in the urine of icteric new-born children* appears to me to be a very weighty objection to the opinion* recently expressed that icterus neonatorum is caused by a rapid destruction of embryonic blood-corpuscles after birth; even in those most severe cases which prove fatal in a few days we find, as already stated (vol. iii, p. 910), an abundance of bilirubin, but no hæmoglobin in the urine and kidneys.

All the urinary constituents hitherto discussed are soluble in water or in watery liquids, and are in reality conveyed in solution by the arteries to the kidneys. But there are also found in the urine undissolved, formed constituents, which may be very considerable in amount, especially under pathological conditions; and we are therefore perfectly justified in asking whether the constitution of the blood also exerts an influence on the kind and number of formed constituents in the urine. A question such as this may even now appear unscientific to many, and would certainly have been held to be so a few years ago, since it was then regarded as an established dogma that soluble substances only can pass into the urine. Now, there is no doubt, it is true, that the formed elements of normal blood are unable to pass the physiological renal filter, so that the presence of red or colourless blood-corpuscles in the urine allows us to infer the certain existence of a disease of the kidneys or of the urinary passages. But what applies to the normal corpuscular elements of blood need not therefore hold good of abnormal ones. As a matter of fact, a number of circumstances have lately been made known, which are greatly calculated to overthrow the old idea as to the absolute reliability of the renal filter. In some experimental investigations carried out in our institute, Rütimeyer* and also Bridges Adams† detected beyond all doubt the presence of *milk-globules* in the urine of dogs, into whose veins milk obtained fresh from the cow and then diluted was introduced; and Wiener‡ observed that animals into whose blood he introduced fluid fat, either directly by a vein or indirectly from the peritoneum or a pleural cavity, regularly excrete *drops of fat* with the urine; Maas,§ also, has had precisely similar experiences in patients who as the result of fracture had acquired fatty embolism of the lungs. Further, Grawitz‖ has detected the passage of *spores of the hyphomycetæ* into the urine of dogs and rabbits, into whose blood he had shortly before injected them in suspension. It should be clearly understood that in these cases the urine was perfectly normal, and that in particular it contained neither albumen nor corpuscles, so that possible damage to the glomeruli could with certainty be excluded; rather we have here to do with a true renal secretion which, so far as we can perceive, is in no respect distinguishable from that of hæmoglobin or of injected albumen. Moreover, the *bacilli of anthrax* are so constantly found, in rabbits and guinea-pigs which have been inoculated with blood containing the virus, to occupy the interior of Bowman's capsules and the lumen of the urinary tubules that the possibility of their passage into the urine is beyond all question; and there are sufficient grounds for stating the same of other varieties of schizomycetes, especially of *micrococci*. This capacity of the organism to rid itself, by means of the renal secretion, not only of dissolved but of organised poisons, may certainly be regarded *a priori* as a valuable contrivance of nature; yet we do not so far know enough of the quantitative relations of this mode of excretion to allow of our at present attributing any great practical importance to it. It has, moreover, its dangers. As regards the tubercular virus, it is at least very probable that its excretion into the urinary passages may be the cause of tubercular disease of the uropoietic system.* Yet we may at present pass over such considerations; the examples adduced are sufficient to enable us to answer the question above raised in the affirmative. Not only the dissolved constituents of the blood, *but some undissolved ones also, are capable of excretion by the kidneys*, and these make their appearance in the urine secreted by healthy kidneys when and because they are contained in the blood.

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* Porak, 'Revue mensuelle de méd. et de chir.,' 1878, pp. 324, 429.

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* Rütimeyer, 'A. f. exper. Path.,' xiv, p. 393.

† H. Bridges Adams, 'Hämoglobinausscheidung in d. Niere,' I.-D., Leipsig, 1880.

‡ Wiener, 'A. f. experim. Pathol.,' xi, p. 275.

§ Scriba, 'D. Zeitschr. f. Chir.,' xii, p. 118.

‖ Grawitz, 'Virch. A.,' lxx, p. 546.

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* Cohnheim, 'Die Tuberkulose vom Standpunkt der Infectionslehre,' 2 Auflage, Leipsig, 1881.

CHAPTER II.

INFLUENCE OF THE BLOOD-STREAM ON THE URINARY SECRETION.

Physiological considerations.—The urine in general rise of arterial pressure.—Hypertrophy of the heart.—Increase of pressure in the glomeruli dependent on local conditions.—Diabetes insipidus.—The urine in general fall of arterial pressure.—Interruptions of continuity of the spinal cord.—Cardiac lesions.—Fall of pressure in the glomeruli dependent on local conditions.—Sclerosis of the renal arteries.—Lead colic.—Eclampsia parturientium.

Impediments to the efflux of venous blood.—Thrombosis of the renal vein.—Cyanotic induration of the kidneys.—The urine in mechanical hyperæmia of the kidneys.—Experiments.—Ligature of the v. renalis.—Narrowing of the v. renalis.—Explanation of the experimental results.—The albumen and blood-corpuscles of the urine in mechanical hyperæmia of the kidneys.—Albuminuria of healthy individuals.—Importance of the epithelium of the glomeruli as regards albuminuria.—Sensitiveness of this epithelium to circulatory disturbances.—Hyaline casts.

SCARCELY less important than the constitution of the blood, as regards the urinary secretion, is the manner in which the blood flows through the vessels of the kidneys, *i. e. the pressure and velocity of the renal blood-stream.* What physiology teaches with reference to this relationship of dependence, you know. The fundamental investigations of Ludwig and his pupils have shown, in the first place, that *the quantity of urine secreted keeps pace with the height of the arterial blood-pressure,* increasing with its rise and diminishing with its fall. And, in the second place, it has been proved by the same researches that the amount of urea excreted is similarly altered in correspondence with the arterial blood-pressure. The excretion of urea does not, however, vary exactly with the excretion of water. On a rise of blood-pressure, the quantity of urine undergoes a greater increase than does the excretion of urea, so that the percentage of urea in the urine is less than before; and on a fall of blood-pressure the rate of excretion of the water becomes less than that of the urea, so that the percentage contents of urea are larger, and the urine becomes more concentrated. Only in the case of very concentrated urine, containing 8 to 13 per cent. of urea, was an exception discovered to this law; here, with the fall of pressure, the rate of secretion of the urea decreased more than that of the water; the urine became more dilute. This exception may, however, be neglected by us since such a high urea-contents is never met with in human urine. These fundamental laws have not been contested during the two decades which have elapsed since their establishment, and apparently contradictory results have been explained as our knowledge of the factors determining the blood-pressure extended. That in this relationship of dependence *the height of the blood-pressure prevailing in the glomeruli* is the real determining factor, was long ago definitely stated by M. Herrmann;* and since it has become known to what variations the calibre of the small arteries of the body is liable, and how important their calibre is as regards the height of the arterial pressure, it is not hard to understand that the heights of the general arterial pressure and of the pressure prevailing in the glomeruli are far from keeping pace the one with the other. Rather, as Grützner† more especially has shown, everything depends on the calibre of the small arteries supplying the glomeruli: if these are sufficiently wide, the pressure in the tufts closely follows the general pressure as measured in the large arteries; if they are narrow, it may happen that, in spite of a very high general pressure, little blood will enter the glomeruli. Hence it is easy to understand that, in many varieties of extreme rise of blood-pressure depending on general arterial spasm,

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[*] M. Herrmann, 'Wien. akad. Sitzungsber.,' Math.-natur. Cl., Bd. xxxvi, p. 349 (1859), xlv, p. 316 (1861).

[†] Grützner, 'Pflüg. A.,' xi, p. 370.

e. g. in electrical stimulation of the spinal cord, in asphyxia, in poisoning by strychnia or digitalis, the urinary secretion is arrested precisely when the rise of pressure is at its highest, and only becomes abundant when the arterial spasm is relaxed, or, should the spasm depend on stimulation of the vaso-motors, when the renal nerves are divided. Moreover, the various changes—by no one more thoroughly studied than by Eckhard*—undergone by the urinary secretion after irritation or division of certain nerve-tracts lose everything of an enigmatical character on considering the influence of these procedures on the blood-pressure.† This is true of the considerable diminution of the quantity of urine, amounting even to complete arrest, which follows division of the spinal cord, as well as of the alteration of the secretion which ensues on section of the splanchnic. For since the splanchnic is the vaso-motor nerve of the kidney, one might expect that its division should increase the secretion; but since its section has at the same time the effect of diminishing the arterial pressure, the increase in the amount of urine may prove very slight, especially in the rabbit, in which the fall of pressure is very considerable; the urine may in fact undergo no increase, or, as in the dog, be extremely variable. Stimulation of the medulla after division of the splanchnics always causes an increase in the amount of urine secreted; after unilateral section only, of course, on the corresponding side. Still less has the division of the nerve-plexus accompanying the renal artery a constant effect on the secretion of urine; for its essential success depends on its rendering the glomeruli accessible to the variations of aortic pressure, and it does not certainly effect this, because the tonus of the small arteries is not dependent alone on the state of excitation of the nerves passing to them from without. When these relations are given their due weight, the assumption of the existence of secretory and secretion-inhibitory nerves in the kidney becomes unnecessary for the explanation of the complicated and apparently paradoxical results of experiment; their existence is so far anything but certainly determined, while the dependence of the urinary secretion on the blood-stream through the kidneys is one of the best established facts of physiology. There can at most be a difference of opinion as to which of the elements in the blood-flow is the really determining factor. Ludwig, in harmony with his theory of filtration, believes it to be the *blood-pressure,* relying mainly on the fact that a lowering of arterial pressure is followed by an arrest of the secretion, even though it still allows the passage of a noticeable quantity of blood through the kidneys. In opposition to this view, Heidenhain,* one of the physiologists who know most of the function of the kidneys, has convinced himself, chiefly on the strength of a fact which will shortly engage our attention, that the determining factor is not the blood-pressure but the *velocity of the stream, i. e. the amount of blood which passes through the vessels of the glomeruli in the unit of time.* It is far from an easy matter to choose between two opinions, each based on such good grounds; and however important the entire question, we pathologists will I think willingly suspend our judgment, above all because, in the great majority of the cases in which we are interested, both the change of pressure and the change of velocity take place in the same direction.

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* Eckhard, various essays by him and by his pupils in the 'Beiträge zur Anat. und Physiol.,' iv—vi.

† Ustimowitsch, 'Ber. der sächs. Ges. der Wiss. M. Phys. Cl.,' 1870, p. 430.

The results of physiological experiment are nowhere contradicted by pathological experience. A permanent elevation of arterial pressure is observed, as you know, in all cases of marked *hypertrophy of the left heart,* when the latter is not merely compensatory of some other circulatory lesion causing a lowering of pressure. In fact, individuals with pure cardiac hypertrophy pass large quantities of thin pale urine which is poor in urea. This is nowhere more strikingly seen than in those cases of hypertrophy of the heart which originate in the train of atrophic processes in the kidney, such as cirrhosis and hydronephrotic atrophy; for here, where it might *a priori* be expected that, owing to the considerable loss of gland-substance, abnormally little urine would be secreted, the high pressure under which the blood reaches the glomeruli and the great velocity with which it passes through the tufts exert such an influence that the amount of urine, instead of becoming less than normal, *mostly exceeds it by a considerable quantity.* A daily volume of 2500 or even 3000 c.c. is very common in such patients, and quantities of 4000 c.c. and more have often been observed. At the same time the urine is of *low specific gravity* (on the average 1010—1012) *because it is poor in solid constituents,* above all in urea; the percentage of urea in the most marked cases is usually between 1 and 2, and may occasionally even be less than 1 per cent. This low percentage of urea, as I need hardly point out, does not in any way involve an absolute diminution in the amount excreted; on the contrary, such patients, in complete harmony with the results of physiological experiment, may produce more urea in twenty-four hours than the normal average quantity; and certainly there is no doubt that, so long as their general condition continues good, such persons excrete an amount of urea which quite corresponds with their diet and mode of living.

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* Heidenhain, 'Bresl. ärztl. Zeitschr.,' 1879, No. 22. Treated at length in Hermann's 'Handb. d. Physiol.,' v, i, p. 309, *et seq.*

Pathology is unable to supply equally pregnant and convincing illustrations of the action of rise of pressure in the glomeruli, *depending on local conditions.* We might certainly here include the compensatory or *collateral* fluxion, by which the loss of some of the arteries of the kidney is compensated and rendered inoperative. The importance of this collateral fluxion will be best brought home to you by the fact formerly referred to (vol. i, p. 130), that, after the extirpation of one kidney in a dog, the same amount of water and urea is excreted as before the operation, the diet being the same—provided there be no rise of temperature or other disturbance of the general condition. This result would be impossible but for the relaxation of at least a number of arterial twigs which are otherwise strongly contracted; and in so far as this is the case, we have here unquestionably a locally conconditioned rise of pressure in the glomeruli. Since, however, in the most favorable event only complete compensation is secured, you will not expect any increase of volume, or other alteration in the constitution of the urine. Hence, your interest will certainly be much more [illegible]y another pathological condition which w[illegible] example of the functional disturba[illegible] engaging our attention—if only it could be shown with certainty that the causal connection is of this kind; I refer to *polyuria* or *diabetes insipidus*. By polyuria we understand a *morbidly increased excretion of urine free from sugar*, which does not depend on serious disease of the kidneys. The amount of urine passed by such patients in twenty-four hours considerably exceeds the physiological standard, and in some cases may be ten or twenty times more than normal. The urine is clear, very pale, and, owing to its richness in water, of abnormally low specific gravity, as a rule between 1004 and 1010; in the most marked cases even these values are not reached. From this fact alone you may gather how small must be the percentage of solid constituents, and more especially of urea; although here too the absolute daily excretion of urea is very considerable, sometimes even abnormally excessive. Grape-sugar is not contained in the urine in diabetes insipidus; on the other hand, inosite, though not constantly present, has been found a few times.* On inquiring by what this remarkable augmentation of the renal activity is caused, we must from the first exclude every suspicion that it is simply the effect of an abnormally abundant supply of water. Were this so, the augmentation would not, of course, be *morbid*; and while it is obvious that the diabetic could not permanently pass such enormous quantities of urine, did they not drink equally large quantities of water, it can be shown of this disease with tolerable certainty that the thirst and enormous water-supply are secondary effects of the polyuria. The occurrence of a primary lasting increase of the sensation of thirst, independent of glycæmia, a true *polydipsia*, is not to be disputed;† yet diabetes insipidus certainly does not depend on such a condition, since it has been found in various cases that the polyuria, though reduced, persists after the supply of water is restricted, and that the patients invariably excrete more water by the kidneys than do healthy persons taking an equal quantity of liquids.‡ We are accordingly compelled to seek the cause of the polyuria in an abnormal condition of the kidneys, and the constitution of the diabetic urine unquestionably reminds one of the secretion which follows an abnormally abundant blood-supply to the glomeruli. Since, moreover, the tension of the larger arteries in these patients is anything but increased, we are led *per exclusionem* to ask, whether a local diminution of resistance in the small renal arteries, an *active hyperæmia* or *congestion*, is not the determining factor here. The congestion may be the result of nervous influences. For the splanchnic contains constrictors of the renal vessels; and although we are unable as yet to follow the course of all the vaso-motor nerves of the kidneys with desirable accuracy, we have only a moment since referred to alterations in the calibre of the renal vessels which may be produced experimentally by the stimulation or division of various nerve-tracts. It perfectly harmonises with this that, in the ætiology of diabetes insipidus, concussion of the brain and other injuries to the skull, violent emotional disturbance, and chronic disease of the brain and spinal cord play an important *rôle*; and also that, in a large number of cases, anatomical investigation has revealed focal disease of the central nervous system, especially in the neighbourhood of the fourth ventricle.* But since the tonus of the small arteries is not exclusively controlled by the vaso-constrictors, their permanent dilatation may depend on other factors, at present unknown, of which we can only say that they are not influenced by the central nervous system. Some such factor must be assumed for the numerous cases of diabetes insipidus in which no disease of the brain can be detected, or indeed any recognisable cause be discovered. You will not, however, conceal from yourselves that it is a perfectly hypothetical view which is here presented you, and because of this I thought it my duty to be most reserved in connecting polyuria with the functional derangements of the kidney here engaging our attention.

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* For details see the text-books of special pathology, *e. g.* Senator, in Ziemssen's 'Handb.,' xiii, Abth. 2, p. 555.

† Cf. the typical case of Nothnagel, 'Virch. A.,' lxxxvi, p. 435, contains references to literature.

‡ Cf. Senator, loc. cit., p. 568.

Much more frequent opportunities are presented at the sick-bed of observing the influence exerted by *diminution of the blood-pressure* in the glomeruli on the urinary secretion.

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* Ibid., p. 564.

The determination of the amount of urine secreted by persons who have sustained an interruption of continuity of the spinal cord is, it is true, attended by certain difficulties, since disturbances in the evacuation of the urine are also invariably present. The few statements contained in the literature agree, however, in this, that after *interruptions* of continuity of the cord at so high a point as to cause considerable lowering of the arterial pressure, the amount of urine excreted is greatly *reduced.* But the true classical examples of altered urinary secretion dependent on low arterial pressure are afforded by the *non-compensated* or *insufficiently compensated cardiac* or *pulmonary lesions.* Here the daily amount of urine is always considerably less than normal. The urine is, at the same time, of high specific gravity, 1024 to 1030 and more, because, in perfect agreement with Ludwig's experiments, the secretion of the solid constituents, more especially of the urea, has not decreased *pari passu* with the water; the urea present in such urine may amount to more than 5 per cent. The urine, owing to its concentration, appears dark red, and for the same reason, though clear when passed, it becomes cloudy on cooling in consequence of a copious deposit of urates. That the urine of persons affected with heart disease actually owes its peculiarities to the diminished arterial pressure may often be proved with the precision of an experiment; for, so soon as the arterial tension is restored to its normal elevation, either spontaneously or by the aid of the physician, there immediately takes place an abundant secretion of urine, whose urea-contents correspond exactly to the food taken, &c. At this time the urine of persons suffering from heart-disease is not essentially distinguishable from that of healthy individuals on the same diet, while during the periods of inadequate compensation it shows a decided resemblance to the urine of pyrexia. In the main it is due to other causes that the urine of fever is scanty and comparatively rich in urea; but when, as so commonly happens in many pyrexial affections, the arterial pressure is low, there is, in addition to the factors previously dwelt on, another which tends to produce a like alteration of the urine.

While in the foregoing cases the low tension in the glomeruli was only a part-phenomenon, an outcome, of the general fall of pressure, there is no dearth in pathology of examples where the deficient fulness of the glomeruli depends solely on *abnormal resistances in the renal arteries*. These resistances must, if their effects are to become apparent in the urine, involve all or the great majority of the small arteries of both kidneys, for otherwise the compensatory influence of collateral fluxion would make itself felt; and hence, for this if for no other reason, in *sclerosis* of the renal arteries we have but rarely the opportunity of observing a diminution of volume of the urine passed in twenty-four hours. To this must be added the facts that sclerosis of the renal vessels is usually complicated by atrophic processes in the parenchyma, and that when it forms a part-phenomenon of extensive sclerosis of the arteries, there is present at the same time either an hypertrophy of the heart or the signs of a general circulatory disturbance. The effect of an abnormal increase of resistance in the renal arteries appears in a much purer form in *lead colic* than would be possible under the circumstances just mentioned. For so long as the superficial arteries are markedly tense, and the colicky pains are violent, the urinary secretion will be reduced, and the specific gravity of the urine, sometimes very scanty, continues high. So soon, on the other hand, as with the relief of the pains, the vascular tension falls, the amount of the urine increases, and here too almost with the promptness of an experiment.* There is also much to be said in favour of the view that the considerable diminution of the urinary secretion, which precedes the paroxysms in *eclampsia parturientium* and regularly persists so long as the attacks continue, depends, in a number of cases at least, on *spasm of the renal arteries*. The spasm, while sufficient to considerably limit the blood-supply to the glomeruli, cannot be so great as to completely occlude the lumen, for then not only would there be complete suppression of the urinary secretion, but profound structural alterations of the kidney could not fail to occur. Anyone, at least, who has often examined the kidneys of women dying during the eclampsia, knows that, at any rate in the cases setting in acutely, there is no question of actual nephritis. Again, the hypothesis of an extreme mechanical hyperæmia, in consequence of the alleged pressure of the pregnant uterus on the renal veins, is, to say nothing of the topographical difficulties, overthrown simply by the fact that the kidneys in eclampsia are far from cyanotic, but as a rule pale; they are certainly not hard, but rather the opposite. Lastly, if the cause of the oliguria be sought in an occlusion of the urinary passages, due either to compression of the ureters or even of the bladder by the uterus, or to the obstruction of numbers of the open urinary tubules by casts, it can only be through overlooking the fact that a kidney which is kept from secreting by resistances in the urinary passages must become œdematous or that a dilatation of the ureter and pelvis must be developed—conditions which as a rule are not found in the kidneys after death from eclampsia. To all these theories, which in the great majority of cases are easily disproved, we may, so far as I see, prefer the hypothesis of an arterial spasm, perhaps of reflex origin, which is the more deserving of respect as it also throws light, as you will shortly hear, on the albumen-contents of the urine in eclampsia.

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* Cf. Riegel, 'D. A. f. klin. Med.,' xxi, p. 175.

The pressure and velocity within a vascular area do not, however, depend solely on the amount of arterial resistance, but are also influenced by the resistance in the *veins*; and we are consequently justified in asking, how does the urinary secretion behave *when the venous efflux is impeded?* Mechanical hyperæmia of the kidney due to *local* obstacles scarcely plays a part in pathology. Not that thrombosis of the renal veins or of the vena cava at the level of the v. renales does not take place. It develops so slowly and gradually, however, that the formation of sufficiently large collateral channels is possible; and thus even total thrombosis of both the main renal veins and of their larger tributaries is always simply an accidental *post-mortem* discovery for which no alteration of the urine *intra vitam* had prepared us; nor is there, as a rule, any structural change in the organs. But the kidneys all the more frequently participate in general venous stagnation, so that so-called cyanotic induration of the organs is one of the most characteristic of the appearances found after death from heart disease, &c. The kidneys are then large and remarkably firm in consistence;

their smooth superficies and the surface on section are blue-red throughout, the pyramids still darker than the cortex; all the vessels are excessively full, especially the veins and the markedly dilated capillary network, while the glomeruli are less strongly filled, though they also contain a large amount of blood. The interstitial connective-tissue, the true stroma of the kidneys, is neither infiltrated with cells nor greatly increased, yet it feels very firm to the touch; and although the epithelia as a rule display no alterations, even when the cardiac lesion has long been present, in the most severe cases *fatty degeneration* may be found in them. While the anatomical effects of permanent venous stagnation in the kidneys can accordingly be accurately defined, the question of the resulting functional disturbances is not so easily decided. For, *pari passu* with the general venous stagnation, there necessarily occurs, in the uncompensated cardiac lesions, a lowering of arterial pressure, whose influence on the urinary excretion has just been described. My description of the urine in these cases was, however, incomplete; I omitted one feature which is never absent in pronounced cases, namely, the presence of *serum-albumen* and *red blood-corpuscles* in the urine. But inasmuch as Ludwig's experiments have not taught us that albuminuria and hæmaturia are regular consequences of a low pressure in the glomeruli, it is natural to suppose that these are effects of the mechanical hyperæmia. As to whether this supposition is well founded, we may expect experiment to afford an absolute decision.

But this decision will not be arrived at as the result of the ligature of the v. renalis, so often practised. When the renal veins are tied in a dog or rabbit, a very considerable swelling is rapidly developed, so that the organ may acquire in less than an hour's time double the size and weight of its fellow. Its colour is throughout a deep red, partly in consequence of the enormous overfilling of all the vessels, and partly from the occurrence of large extravasations of blood. Whether rupture of some of the vessels takes place must remain undecided: as in all cases of mechanical hyperæmia so here, the extravasation depends essentially on *diapedesis*. On microscopical examination the lymph-spaces of the kidneys are observed to be filled with blood-corpuscles, which are in some places collected into small clumps, perceptible to the naked eye as punctiform hæmorrhages. Innumerable blood-corpuscles also lie in the lumina of the urinary tubules, the open tubules of the medulla being actually plugged with them. When this stage has been reached—which regularly occurs in from one to two hours after ligature of the veins—not a drop of urine can be obtained from a cannula bound into the ureter, and if the ureter be examined it is not uncommonly found filled with a soft blood-clot. Not so at the beginning of the experiment. Immediately after occlusion of the veins, there drops from the cannula a bloody fluid rich in albumen, which, at first only moderate in quantity, soon begins steadily to decrease, till finally the secretion dries up altogether. There is, in my opinion, little interest in discussing the elevation reached by the pressure in the glomeruli as the result of this procedure, or the extent to which the lumina of the open tubules are encroached upon by the congested veins of the medulla. For that a gland whose circulation is so seriously disturbed as must be the case after sudden occlusion of the venous efflux and after an operation which, as I formerly stated (vol. i, p. 209), must always be followed by great atrophy of the organ,—that the kidney, I say, should soon refuse to perform its function, does not appear specially remarkable. It is also doubtful enough whether the fluid which, immediately after the ligature, drops from the kidney into the ureter is actually urine, and not rather the lymph of stagnation; and at any rate it is obvious that an experiment such as this is absolutely worthless so far as the theory of urinary secretion is concerned.

If the experimental increase of venous pressure is to give really useful results, it must consist of nothing more excessive than a narrowing of the vena cava above the renal veins, or still better of the vena renalis itself, as in the method employed by Robinson and more recently by Perls and Weissgerber.* In this instance, also, *the amount of urine immediately begins to decrease*, though not nearly in the same degree as when the occlusion is complete, and never to the extent of total suppression. At the same time the scanty and concentrated secretion soon becomes albuminous, and a microscopic examination of the slight sediment reveals even after a few hours *a number of red blood-corpuscles and a few hyaline casts.* As far as the fact itself is concerned, it is thereby sufficiently established that the urine in heart-disease owes a good part of its characteristic peculiarities to the mechanical hyperæmia, but the explanation of the fact is not so easy. As regards the decreased amount of urine, in the first place, this is the point, already alluded to, which essentially influenced Heidenhain in formulating the theory of velocity as opposed to the pressure hypothesis. On more closely considering the effects of the narrowing of the renal veins on the renal circulation, we can have no doubt that a rise of pressure will take place, chiefly in the network of capillaries surrounding the convoluted tubes ; and if the tension in the vas efferens were the same as in the small arteries of the remainder of the body before they break up into capillaries, it would be questionable even whether the vessels of the glomeruli would experience any increase of pressure through interference with the venous efflux. This, however, is not the case ; and because the tension in the efferent is considerably lower than that in the afferent artery, the increased tension must be propagated from the veins on into the glomeruli, though in less degree. Nevertheless, the diminution of the urine in mechanical hyperæmia does not appear to me to be a sufficient argument against the pressure hypothesis. For, as you are aware, the determining factor according to this hypothesis is not the absolute height of the pressure in the glomeruli, but the difference between the pressures in the glomeruli and urinary tubules ; and, on bearing in mind that in the kidney, provided as it is with a rigid capsule, the overloaded and abnormally distended vessels must necessarily everywhere compress the tubules, but more especially in the medulla,* you will find no difficulty in believing that, in spite of the increased pressure in the glomeruli, the difference of pressure in them and in the urinary tubules may yet be diminished in venous stagnation. On the other hand, I do not fail to perceive that the mechanical hyperæmia may prove a serious obstacle to the circulation in the glomeruli, and must thus reduce the velocity of the blood-stream through them.

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* Robinson, 'Med.-Chir. Transact.,' vol. xxvi, p. 51; Weissgerber und Perls, 'A. f. experim. Pathol.,' vi, p. 113.

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* C. Ludwig, 'Wien. akad. Sitzungsber.,' Math. naturw. Cl., Nov. 5, 1863.

Still greater interest perhaps attaches to the second peculiarity of the urine in mechanical hyperæmia, to the symptom, *i. e.* which plays so great a part in the pathology of the urinary apparatus, namely, the *passage of normal albumen and corpuscular elements from the blood into the urine.* For to say nothing of the red blood-corpuscles, the albumen of the urine in mechanical hyperæmia is regular *serum-albumen;* and although the number of blood-corpuscles is not very great and the amount of albumen never exceeds one or two parts in the thousand, it is yet necessary to learn the conditions allowing of the passage into the urine of constituents of the blood which do not escape in a physiological condition. It is hardly possible to arrive at a proper decision of this question on *a priori* grounds, that is, by considering our other experiences with regard to mechanical hyperæmia, as observed in the remaining organs and vascular areas of the body. These could only lead us to conclude that, instead of the ordinary transudation from the small vessels of the medulla and capillaries surrounding the convoluted tubes, there escapes during the hyperæmia a large quantity of lymph containing blood-corpuscles but poor in albumen, which entering the lymph-spaces of the kidney, leaves the organ through the large lymphatics of the hilus. But owing to the dearth of similar experiences as regards the other glands, it would be impossible to say whether the lymph becomes mingled with the renal secretion by forcing its way through the wall into the lumen of the urinary tubules. On the other hand, the albumen may pass directly from the glomeruli into the urinary passages, though it may be questioned whether the rise of pressure in them is great enough in ordinary stagnation to force through them the typical lymph of mechanical hyperæmia. To decide between these possibilities, Senator* modified the experiment by reducing the time of the occlusion of the veins to a very short period, about ten to twelve minutes, and then at once removing the kidney from the living animal. On then, according to Posner's method,* throwing the kidney into boiling water to fix the albumen transuded, it was easy to detect *masses of coagulated albumen and also blood-corpuscles in the lumen of some of the straight tubules, chiefly of the medulla,* while the capsules of Bowman remained *absolutely free.* Should these results, which were obtained exclusively on rabbits, be confirmed for other species also—as is *per se* very probable—it would hardly be possible to raise an objection to the conclusion of Senator,† that in mechanical hyperæmia the lymph, *i. e.* the dissolved albumen and the blood-corpuscles, exude first from the abnormally distended capillaries surrounding the tubules into the lumen of the latter and mingle with the urine. True, it does not stop short at this. Rather, if the mechanical hyperæmia be kept up longer, masses of albumen and blood-corpuscles make their appearance also within the capsules, and the number of capsules so changed increases in proportion to the time that has elapsed since the vein was occluded.

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* Senator, 'D. Albuminurie im gesunden und kranken Zustande,' Berlin, 1882, p. 56.

Anyone who desires to understand this passage of the serum-albumen from the glomeruli into the commencements of the urinary tubules must first of all answer the question, How comes it that the urine, the greater part of which at least is excreted through the glomeruli, is normally non-albuminous, while all the other transudations of the body contain albumen, although in different proportions? True, I must not conceal from you that doubts have recently been raised as to the absolute truth of the rule that normal urine is free from albumen. It is long since isolated observations were recorded, according to which albuminous urine might be secreted by persons with healthy kidneys, sometimes as the result of emotional disturbance, of bodily exertion, or of the consumption of food, but occasionally in the absence of any such cause; and more recently the systematic examination of the urine of healthy individuals by means of more delicate methods has directed attention to the fact that an unmistakable, though trifling, amount of albumen may be observed with comparative frequency in the urine of perfectly healthy persons:

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* Posner, 'Virch. A.,' lxxix, p. 311.

† Cf. the statements bearing on the point in Senator's 'Albuminurie,' p. 16, *et seq.*; and of Wagner in Ziemssen's 'Handb.,' ix, 1, 3 Aufl., p. 24.

Leube,[*] Munn,[†] Fürbringer,[‡] and others found that one out of seven or eight healthy individuals had undoubted albuminuria. This, I do not fail to perceive, is a very high average, and even if we make a deduction for cases of latent renal disease, it remains surprisingly great; but to proclaim on this account with Senator[§] that albuminuria is a *physiological* occurrence which only escapes notice owing to the insignificant albuminous contents, is not, in my opinion, justifiable. Leube, who detected albumen in the urine of 16 per cent. of the 119 soldiers examined by him, does not come to this conclusion, but, on the contrary, is inclined to attribute the fact to individual differences in the membranous covering of the glomeruli. At any rate, it would only be necessary to modify the question to the extent of asking how it happens that a fluid is excreted from the glomeruli which, unlike all the other transudations from the capillaries of the body, contains such a small quantity of albumen that in the great majority of individuals it cannot be detected even by the most delicate methods. Now, even if one be not disposed to follow Heidenhain in his view of the structure of the kidney so far as to regard the epithelia of the Malpighian tufts as *active secretory elements*, whose material is supplied by the vessels of the glomeruli, it is yet, in the present state of our knowledge, *impossible to avoid ascribing to the layer of epithelium covering the glomerulus the function of keeping back the albumen.* That this layer of epithelium is actually qualified to arrest certain constituents which the loops of the glomeruli let pass, is supported, as Heidenhain has rightly pointed out, by the well-known markings presented by the kidneys in argyria; for the fine granules of silver are here met with *outside the vascular loops*, it is true, but not lying free in the interior of the capsule or of the tubules; they are contained in the cells of the epithelial covering of the glomeruli. This membrane is quite peculiar to the glomeruli, and were it absent it would be impossible to see why the vascular tufts, perfectly resembling as they do in structure all other capillaries, should not like them allow a markedly albuminous fluid to transude. That the Malpighian tufts must be peculiar was instinctively recognised before the epithelial covering was accurately known; these vessels were asserted to possess a peculiar impermeability to serum-albumen which, according to the then current conceptions as to the laws regulating the filtration of albuminous fluids through membranes, could not withstand an increasing filtration-pressure. How this purely theoretical notion could so long remain master of the field, in spite of the fact that it was unsupported by any pathological or experimental evidence, is really difficult to understand. Division of the splanchnic or of the renal nerves is not followed by albuminuria, provided the renal nerves be divided carefully without stretching or crushing of the renal vessels. Nor does albuminuria set in on the non-innervated side in asphyxia, much less in the inconsiderable rise of blood-pressure which is produced by tying the aorta below the renal arteries, or the aorta together with the subclavians. Pathological polyuria also generally runs its course without albuminuria; persons with idiopathic, it may be nervous, cor bovinum do not exhibit it, so long as their general state is good; and if the urine of persons with cardiac hypertrophy consequent upon cirrhotic kidney, as a rule contains a slight amount of albumen, the different inflammatory changes still taking place in such kidneys are such a sufficient cause of albuminuria that the temporary or permanent absence of albumen from the urine, which has repeatedly been observed, affords striking testimony to the impotence of the high blood-pressure. More recently, the supposed theoretical foundation of this view has been seriously weakened by the experiments of Runeberg* on the filtration of solutions of albumen, to which reference has already been made (vol. i, p. 514). He found that *when the filtration-pressure is augmented the percentage albuminous contents of the filtrate decrease, and vice versâ*, as well as *that the permeability of an animal membrane to albumen and to particles in suspension increases when the escape of the filtrate is prevented*, and the opposing pressure external to the membrane is in consequence raised. On that occasion I dwelt on my objections to Runeberg's experiments, and more especially on the reasons why I do not regard it justifiable to apply his results without more ado to processes taking place in the living body. I also drew attention to the fact that our experiences with regard to the transudation of stagnation do not agree with those experimental results. My objections have not been overcome by the subsequent highly interesting publication of Runeberg,* in which he attempts to explain our clinical experiences of albuminuria on the basis of his filtration-experiments. Add to this what I also then mentioned, that Runeberg's interpretation of his experiments, though not the facts themselves, have been attacked by several persons.† Everything considered, you will easily understand that I cannot regard this writer's view, according to which the albuminuria is dependent on a fall of pressure in the glomeruli, as being as yet established. I am the less inclined to accept it, since the albuminuria setting in under these circumstances may be explained in a very different way, namely *by an alteration in the constitution of the membranes concerned in the excretion of urine.*

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[*] Leube, 'Virch. A.,' lxii, p. 145.

[†] Munn, 'New York med. Rec.,' March, 1879.

[‡] Fürbringer, 'Ztschr. f. klin. Med.,' i, p. 340.

[§] Cf. the statements bearing on the point in Senator's 'Albuminurie,' 5, *et seq.*

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* Runeberg, 'A. d. Heilk.,' xviii, p. 1.

That the Malpighian tufts are very sensitive to disturbances of the circulation is a tolerably old experience. Hermann was the first to observe the fact, afterwards more carefully studied by Overbeck,‡ that even a short interruption of the renal blood-stream is followed by a suppression of the urinary secretion, lasting from a few minutes to three quarters of an hour, while the urine subsequently passed contains a few red blood-corpuscles as well as *albumen,* and continues to do so for some hours or days, according to the duration of the ischæmia. In perfect agreement with this is the circumstance that when the renal secretion recommences after an *attack of cholera,* the urine invariably contains albumen for a time; and in like manner lying-in women who have recovered from eclampsia always pass albuminous urine after the anuria has subsided. Yet complete interruption of the circulation is not necessary for the production of this result. Hermann detected albumen in the urine after compressing the renal artery so as still to allow the blood, though in greatly diminished quantity, to reach the kidney; and in cholera and puerperal eclampsia the urine may become albuminous before suppression, *i. e.* in the stage of oliguria, at a time when the blood-stream through the kidneys is diminished but not arrested. Whether, with Heidenhain, you will attribute the temporary arrest of the urinary secretion, following a transitory interruption of the circulation, to a secretory incapacity of the epithelium of the glomeruli, I must leave to your own discretion; in my opinion, however, it may unhesitatingly be inferred from these experiences *that every considerable circulatory disturbance renders the membranes concerned in the excretion of urine permeable to albumen.* While Overbeck thought of an alteration in constitution of the entire glomerulus, we, who do not doubt the normal permeability of the capillary loops for albumen, shall refer their abnormal permeability to an alteration of the glomerular epithelium.

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* Runeberg, 'D. A. f. klin. Med.,' xxiii, p. 41, 225.

† Heidenhain, in Hermann's 'Handb. d. Physiol.,' v, 1, p. 368, *et seq.*; Gottwalt, 'Ztsch. f. phys. Chemie,' iv, p. 423.

‡ Overbeck, 'Wien. akad. Sitzungsber.,' xlvii, Abth. ii. p. 189.

If, accordingly, we assume that the glomerular epithelium loses its capacity of keeping back the serum-albumen whenever an abundance of fresh arterial blood fails to be supplied to the vascular tufts, we have a ready explanation of many pathological varieties of albuminuria. We have only this moment considered the albuminous urine of cholera and of eclampsia; it is probable, however, that the albuminuria so often observed after an *epileptic attack* and in *tetanus* is the consequence of temporary tetanic contractions of the small renal arteries, and this is certainly the case with the albuminous urine not rarely seen in *lead colic.* From this point of view, moreover, it is easy to understand that stretching or crushing of the main renal arteries will, as already indicated, be followed by albuminuria. While in these cases the circulatory disturbance in the glomeruli is conditioned by an abnormal state of the vessels supplying them with blood, a general fall of arterial pressure may also result in the glomeruli being inadequately fed. This factor assuredly makes itself felt in the albuminuria which almost invariably accompanies *septic* and all other *pyrexial diseases* attended by a lowered tension of the arterial system. The occasional presence of albumen in the urine in cases of *pernicious anæmia* and *leukæmia* need hardly be referred to any other cause; and that this is the origin of the albuminuria following the application to the skin of an impermeable coating appears to me to follow from the fact that the symptom sets in in those animals only whose temperature and entire circulation are unfavourably influenced by the operation, *e. g.* rabbits, but not in dogs or in man.* Finally, to return to the point from which we set out, our assumption completely explains the albuminuria of venous stagnation, whether due to local causes or to general conditions such as attend non-compensated cardiac lesions; for in both instances the blood of the glomeruli can only with more or less difficulty be renewed, in purely local hyperæmia owing to the obstacle to the efflux of blood, and in cardiac lesions because of this and also of the abnormally reduced supply.

But since the conditions determining all these varieties of albuminuria are analogous, though their fundamental causes differ, the urine presents in all approximately the same appearance. At least it is scanty, acid, of a deep colour (except of course in anæmic individuals), and has a slight albuminous contents. Only the urine of cholera and of eclampsia, as well as that passed after complete closure of the artery, are wont to contain an abundance of albumen; in the remaining forms there is never more than one or at most two parts in the thousand, and even these values are frequently not attained, only a moderate cloudiness being produced on boiling, with the formation of a few delicate flakes when the urine is allowed to stand. Within these limits, the variations in the albuminous contents correspond pretty accurately to the duration and intensity of the circulatory disturbance; or, in other words, *the glomerular epithelium becomes more permeable to albumen the less the quantity of arterial blood flowing through the tufts in the unit of time.* This formulation harmonises at any rate with the explanation of these forms of albuminuria adopted by us, while Runeberg explains them from his standpoint as due to a decrease of the filtration-pressure or—in venous stagnation—to a rise of counter-pressure. At bottom it would almost appear, however, as though the difference between the two views were not so important;

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* Senator, 'Virch. A.,' lxx, p. 182.

for, according to Runeberg also, the process of filtration is affected by the variations of pressure and counter-pressure simply because the pores of the membrane become larger or smaller,—because, that is, the constitution of the membrane is altered. Nevertheless, the contrast between the two assumptions is obvious. If in the kidneys we had to deal solely with *physical* alterations in the condition of the glomeruli, it is evident that, on the restoration of the normal circulation, the albumen must at once disappear from the urine, while from our, so to speak, *biological* conception, it follows that a secretion of non-albuminous urine will not take place till the glomerular epithelium has been restored by the renewed supply of an abundance of blood to the vascular tufts. Such after-effects do, as a matter of fact, present themselves. Thus it was found, in Overbeck's experiments, that many days may sometimes elapse before the urine becomes free from albumen, and on convalescence from cholera the urine is normal in amount before the last traces of albumen have disappeared from it.

That the urine of venous stagnation and of ischæmia contains *blood-corpuscles* as well as albumen, has been repeatedly stated. The quantity of blood-corpuscles present is determined essentially by the intensity and duration of the circulatory disturbance. They are consequently most numerous in the portions of urine first passed after an attack of cholera and in the secretion of persons suffering from heart disease—with this difference, that, in accordance with the form of circulatory disturbance, there is a preponderance of red blood-corpuscles in the urine of mechanical hyperæmia, while in that of convalescents from cholera and of eclampsia colourless cells are also present. But the urine in these cases as a rule contains still more interesting structures—so-called *urinary casts*. By urinary casts we understand, as is well known, *masses of albumen*, which have acquired a solid aggregate condition inside the renal tubules, and have at the same time accommodated themselves to the lumina of the tubules. They may afterwards be washed from the spot in which they were formed into the deeper collecting tubes and thence into the pelvis of the kidneys, and be ultimately evacuated with the urine. In the sediment thrown down in the affections under discussion, they are found as *solid cylinders*, differing greatly in length and breadth, or rather in thickness, and also—what is more important—in colour and general appearance. In the urine in question, except that of cholera, the consideration of which may be advantageously postponed till we come to discuss nephritis, the casts are almost exclusively *hyaline; i. e.* they are pale, almost homogeneous cylinders with a very delicate outline and feeble powers of refraction, and are always few in number. In the kidney they are usually met with in the straight tubules, both narrow and wide, most numerously in the pyramids. Such hyaline casts are contained in small numbers in the urine of pyrexia, in that passed during lead colic, after an epileptic seizure, and especially in the urine of mechanical hyperæmia. As to the origin of the hyaline casts, there need be little hesitation, so far as I see, precisely in their case, in regarding them as derived from the albuminous transudation of the glomeruli. The epithelium of the urinary tubules is, at least in fresh cases, perfectly intact, and in experimentally produced mechanical hyperæmia as well as in fever, the casts make their appearance during the first day in the urine. As against this view, it has been pointed out that the transudation in venous stagnation is invariably distinguished by its feeble coagulability;* but, in the first place, it accords with this that the casts are so few as compared with their number in true nephritis, and, in the second place, we have not in the urine of mechanical hyperæmia to deal alone with the ordinary transudation. That coagulation should take place as soon as dissolved albumen and corpuscular elements reach the urinary tubules does not appear to me to be anything remarkable, while the fewness of the casts seems to perfectly correspond with the scanty transudation of albumen and blood-corpuscles.†

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* Senator, 'Virch. A.,' lx, p. 476.

† On the subject of this and the following chapter compare further the various works on renal diseases, as well as Bartels, in 'Ziemssen's Handbuch,' ix, Abthl. 1, and above all Traube's 'Ges. Abhandl.,' i, ii, 1871, iii, 1878.

CHAPTER III.

THE CONDITION OF THE SECRETORY MEMBRANES.

Nephritis.—Ways by which the exciter of inflammation may reach the kidneys.—Unequal distribution of all forms of nephritis.—Glomerulo-nephritis.—Its influence on the secretion.—Albumen of the urine.—Anatomical description of these kidneys.—Ætiology.—Explanation of the condition of the urine.

Artificial necrosis of the epithelium of the urinary tubules.—Acute Bright's disease.—Anatomical description.—Ætiology.—The urine in acute nephritis.—The various kinds of urinary casts.

Chronic nephritis.—Causes of chronicity.—Anatomico-histological appearances in chronic nephritis.— Chronic hæmorrhagic nephritis.—Granular kidney.—The urine in chronic inflammation of the kidneys.—Cardiac hypertrophy of nephritis.—Theories of Traube, of Gull and Sutton, of Senator, and of Buhl.—Chemical theory of Bright and others.—The theory of water-retention.—Explanation of the hypertrophy of the heart from the circulatory disturbances in the kidneys.—Experiments.—Frequency of hypertrophy of the heart in chronic nephritis.—Compensatory effect of the cardiac hypertrophy on the urinary secretion.—Disturbance and non-occurrence of compensation.—Amyloid degeneration of the kidneys.—Anatomical appearances of the amyloid kidney.—The urine in pure amyloid kidney.—Amyloid albuminuria.—The urine in amyloid nephritis.—"Butter" kidney.—Amyloid contracted kidney.

Purulent nephritis.—Colonies of micrococci in endocarditis ulcerosa and septic processes.—Pyelonephritis.—Renal abscess.—The urine of suppurative nephritis.—Tubercular nephritis.

The urine in cholera.—Explained from the circulatory disturbance occurring during the attack.—Chyluria.—So-called hæmatogenous albuminuria.

Pathological conditions of the epithelium of the urinary tubules.

In the foregoing discussion we have already considered the change undergone by one of the membranes employed in the secretion of urine, a change which, it is true, is itself to be regarded as the result of circulatory disturbances. But, in addition to the glomerular tufts and their epithelial covering, other membranes, both vascular and epithelial, have to be taken into account: amongst the former we have to consider the capillary network surrounding the tubules as well as the larger vessels, more especially the vasa recta; while of the latter the epithelial covering of the urinary tubules, and principally that of the tubuli contorti, must be dealt with. Besides the alterations already discussed, the secretory membranes are liable to others of a different and much more severe character, which are not the effects of circulatory disturbances, but, on the contrary, bring about serious alterations in the blood-stream. In commencing the study of the influence of these alterations on the secretion of urine, we enter a domain in which the results of physiological experiment can only be of service as a foundation and guide to our discussions. For the office of the physiologist is at an end when he has succeeded in referring to each of the factors engaged in the normal process of secretion its proper share in the work, while the disturbances of function dependent upon the abnormal behaviour of these factors have for him a merely subordinate interest. It is all the more incumbent upon the pathologist to concern himself with these disturbances of function, as you will readily admit on calling to mind that the entire group of *inflammations of the kidneys* is included amongst them.

Owing to the deep and protected situation of the kidney it is very rarely injured, while simultaneous injury of both kidneys has almost never been observed. Indeed, traumatic inflammation is the very last form that is suggested by the word "nephritis." An injury of the kidney usually causes the mortification of a smaller or a larger portion of the organ, and at the same time, as a rule, the laceration of some of the vessels. The ensuing inflammation is either very moderate in intensity, leading to the filling up of the defect by cicatricial connective tissue, whilst the necrotic tissues are gradually absorbed, or, if its course is less favorable, it becomes purulent, a *renal abscess* is formed. The immediate effect of the injury is, accordingly, the presence for some time of *blood* in the urine; but when the traumatic hæmaturia has passed off and the case progresses favorably, the urine no more betrays, by any striking symptom, the presence of the slight circumscribed inflammation than it does during the disappearance and healing of a simple embolic infarct. As for the manner in which the renal function is influenced by traumatic abscess of the kidney, this will be discussed later on in connection with certain forms of purulent inflammation which do not arise in consequence of a trauma.

There are only two paths by which an exciter of inflammation can reach the kidneys; *by means of the blood-stream or through the ureter and pelvis.* As regards the first path, the kidneys are disposed, perhaps more than any other organ, to inflammations so brought about, because they are the channels through which are excreted the noxious materials which have in any way entered the juices of the body and are not therein destroyed or otherwise disposed of; this applies above all to matters in solution, but also, as we have seen, to some formed ones. Though this excretion of poisons and other noxæ is highly advantageous to the body, it is yet, as I recently pointed out, attended by danger to the kidneys. Not that all such excretion and every passage of foreign substances through the kidneys are dangerous to these organs. On the contrary, curare, morphia and quinine, iron and iodine, indigo-blue and carmine, milk-globules and olive oil or other indifferent neutral fats—in short, the great majority of all dissolved and formed constituents pass over into the urine without injuring the kidneys in the slightest. There is, however, a number of substances which do not behave so innocently, but, *during their passage through the kidneys, produce* more or less *disturbance of the integrity of the epithelia or vessel walls.*

On attempting to follow in detail the possibilities thus arising, we find that the first part to be seriously exposed is the *glomerulus with its epithelial covering*. Whether a further distinction must here be made, *i. e.* whether substances occur which are adapted to injure only the walls of the vascular tufts or the epithelium alone, the present state of our knowledge does not, in my opinion, allow of our forming a proper judgment. That one is possible without the other, I do not doubt; yet the distinction is without practical importance, since every considerable alteration of the one part gives rise to a change in the other. The next to be threatened is the *epithelium of the tubules*, and chiefly of course of the *tubuli contorti*. For the substances which have filtered through the glomeruli at once come into contact with the convoluted tubes, and may then impair their integrity just as they previously did that of the glomerular epithelium. The noxious materials may, however, reach the epithelium of the urinary tubules in another way. Any one at least who regards as convincing the evidence brought forward by Heidenhain in his well-known essay,* that certain substances, *e. g.* sodium sulphindigotate, are excreted solely by the epithelial cells of the urinary tubules, must also reckon with the fact that the noxæ in question alter the epithelium as they pass through it. In this case they must first have passed through the corresponding capillary network, the walls of which may also become affected during the transudation. This of course need not necessarily happen; rather there is much to show that the epithelium is more sensitive than the capillary walls. On the other hand, it must not be forgotten that severe damage to the epithelium of the tubules will very quickly influence the capillaries in immediate contact with them. As a necessary supplement to the foregoing considerations, will you bear in mind that normally *the renal vessels are never all equally supplied with blood*, nor are all the tubules equally utilized in secretion? For the consequence of this is that the exciter of inflammation never at the same time affects each and all of the glomeruli or urinary tubules, so that the occurrence of *a nephritis involving every part of both kidneys equally can hardly occur*. As a matter of fact, you will very shortly hear that the so-called acute diffuse nephritis more especially is certainly not diffuse, but on the contrary is characterised by an accumulation more or less great of *circumscribed inflammatory foci;* and even in the exquisitely chronic forms, the great variety of the appearances in different portions of the kidneys points to the unequal origin and development of the process.

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* Heidenhain, 'Pflüg. A.,' ix, p. 1.

While, then, the exciter of inflammation first affects the glomeruli, we are sufficiently accurately acquainted with the nature of inflammatory disturbance of the circulation to estimate in the main its influence on the secretion of urine. *Owing to the fall of blood-pressure and decrease of velocity* inseparable from every inflammation, *which take place in the glomeruli, the amount of urine secreted must necessarily be reduced,* and the urea-contents and hence the specific gravity be relatively great. We formerly saw that the glomerular epithelium becomes permeable to albumen when the blood-pressure is low, and to this factor must now be added *the abnormal perviousness of the inflamed vessels,* both of which together *allow the escape of considerable quantities of albumen and corpuscular elements from the blood into the urine.* The urine may accordingly be described somewhat as follows: it is always diminished in volume as compared with the normal, especially at the commencement of the disease, and sometimes to such a considerable degree that only a few hundred cubic centimetres are passed in the twenty-four hours. Its reaction is very acid; its specific gravity relatively high; its colour deep orange to red-brown, or an intense blood-red if many red blood-corpuscles are present. It invariably contains albumen, and in much greater quantities than the urine of mechanical hyperæmia or pyrexia; four to five per thousand is something very common, but it may amount to 1 per cent. or even considerably exceed this. The albumen of this urine consists for the most part, but not exclusively, of *serum-albumen;* other albuminous bodies, resembling *peptones,* which do not coagulate on boiling, and *globulins* may usually be detected in it. Yet this is not a characteristic of this form of nephritis only, for in all the other varieties the urine also usually contains both serum-albumen and the other albuminous bodies just mentioned; whether in equal amount we do not know. The decision of this undoubtedly not unimportant question must be left to the future, since previous investigations* have failed, not so much owing to imperfection of the chemical methods as to the uncertainty of the clinical diagnosis. Furthermore, the urine is cloudy, and deposits on standing a fairly abundant sediment, which, in addition to urates, consists of white and red blood-corpuscles, together with casts, either hyaline or containing blood-corpuscles and consequently coloured. Both kinds of blood-corpuscles are invariably present in the sediment, but their number and especially their relative proportions are very variable. In general it may be said that the quantity of red blood-corpuscles increases with the severity of the disease. The vast majority of the casts are hyaline, and the granular and epithelial varieties are just as rare here as are fattily degenerated epithelial cells and compound granular corpuscles.

The appearances presented by the kidneys post mortem are not what might be anticipated from the condition of the urine; and many a one who, judging from the urine passed during life and the other symptoms, has expected to see in these cases a typical Bright's kidney, has left the post-mortem room with a feeling of disappointment. The kidneys are scarcely enlarged and of normal consistence: they are sometimes a vivid red on the surface as well as on section, but more frequently the cortex has a greyish-violet hue, with which the bluish-red pyramids in a measure contrast. The glomeruli are as a rule clearly discernible as red dots, and in addition to them red points and streaks are present here and there. On microscopic examination, a more or less large number of the same hyaline casts, which are regularly found in the urinary sediment, are met with, chiefly in Henle's loops and the collecting tubes. Still more striking is the presence of red blood-corpuscles; these are aggregated into smaller or larger cylindrical clumps, occupying the lumina of the convoluted, and more especially the straight collecting tubes.

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* Lehmann, 'Virch. A.' xxxvi. p. 125; Gerhardt, 'D. A. f. klin. Med.,' v. p. 212; Edlefsen, ibid. vii. p. 67; Senator, 'Virch. A.' lx. p. 476, and at greater length in 'D. Albuminurie im gesunden und kranken Zustande,' Berlin, 1882, Kap. 11; Fühy-Snethlage, 'D. A. f. klin. Med.' xvii. p. 419; Petri, 'Versuche zur Chemie des Eiweissharns,' Inaug.-Dissert., Berlin, 1876; Wassilewsky, 'Petersb. med. Wochenschr.' 1878, No. 21; Heynsius, 'D. A. f. klin. Med.,' xxii, p. 435; Lépine, 'Revue mensuelle,' 1880, p. 335.

This latter, however, is not a constant appearance, and cannot be anticipated with certainty unless the urine has betrayed by its colour its richness in red corpuscles. The epithelium of the urinary tubules has a somewhat granular aspect; a few fat drops may be noticed here and there, especially in the cells of the convoluted tubes, while a slight multiplication of the nuclei may perhaps be present in some parts of the interstitial tissue. But on the whole *neither the epithelium nor the interstitial tissue presents any change worth mentioning.* As to the parts which might *a priori* be expected to show striking changes, namely, the glomeruli, there is not much to record of a pathologico-histological character. Epithelial defects are occasionally observable in them, and it is possible, further, that the swelling and loosening of the glomerular epithelium, described by several writers,* is a constant, or at least frequent, appearance in these kidneys; I myself have seen little of it in the cases examined by me, but do not wish to attach much importance to these negative results. Yet though, as we have seen, the anatomical alterations presented by these kidneys, and in particular by the glomeruli, are trifling in character, I have no fear that you will regard the organs as perfectly intact and physiological. For you are perfectly aware that in fresh inflammations the microscope fails to discover any distinct alterations of the vessels, so that the existence of the alterations must be inferred from their effects, chiefly, that is, from the abnormal exudation. That such takes place from the glomeruli of the kidney is unequivocally proved by the urine, and you will, I believe, think me justified in proposing for this form of inflammation of the kidney the term pure "glomerulo-nephritis."

You will have few opportunities of examining this form of nephritis anatomically, since it is only exceptionally that the patient dies from it. In reply to the question, however, under what circumstances it occurs, we may say that its most typical illustration is offered by *scarlatinal nephritis.* I do not, of course, refer to the slight albuminuria which, as in so many other pyrexial diseases, appears at the height of the process; I have in mind those cases in which the urine acquires the above-described characters after the lapse of two or three weeks, or at any rate of a considerable time, from the fading of the exanthem. It was on a few rapidly fatal cases of this kind that the foregoing description of the kidney was based. This *glomerulo-nephritis*, besides following scarlet fever, also sets in, though much more rarely, in the train of other *infective diseases*. Thus it may occur after diphtheria, after relapsing fever, after erysipelas and pneumonia; it is also occasionally observed as a sequela to carbuncle or to septic phlegmonous inflammation. Whether this form of nephritis occurs as an independent primary disease, *e. g.* as the result of wetting or chilling of the skin, appears to me probable enough, though I am unable to certainly affirm it, since I know of no post-mortem of the kind. I have, however, seen it in exquisitely typical form in a man whose skin was several weeks before death smeared and rubbed with *petroleum* for four days.*

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* Klebs, 'Handb. d. patholog. Anat.,' i, p. 644; Litten, 'Neue Charité-Annalen,' iv, S.-A., p. 32; Langhans, 'Virch. A.,' lxxvi, p. 85.

But even though glomerulo-nephritis is rare in comparison with the other forms of nephritis immediately to be described, its theoretic importance is not, I believe, at all lessened thereby. These kidneys are excellently adapted for the elucidation of the causal connection of many symptoms. As regards the *reduced volume of the urine*, in the first place, this sign, characteristic of many renal inflammations, has been explained as due either to a compression of the urinary tubules by interstitial exudations, or to a narrowing of the lumina of the tubules through swelling of the epithelium, or again to an occlusion of the tubules by casts. Now, in glomerulo-nephritis every one of these assumptions must be rejected. The epithelium is not swollen; the interstices are not widened; while as regards the presence of the casts in the interior of the tubules, I recently remarked (vol. iii, p. 1129) that, in my opinion, the connection is exactly the reverse; *it is not because the casts occupy the tubules that the urinary secretion is reduced, but it is because the urinary secretion decreases that the casts are disposed to remain seated in the tubules.* The truth of this appears, I think, most clearly when the disease takes a turn for the better; for although the tubules are plugged by large numbers of casts, the increase in the urine is sometimes very abundant; the more powerful urinary stream easily washes away the casts. On the augmentation of volume, the deep colour of the urine is exchanged for a paler, and the specific gravity falls to 1010 or less,—telling evidence that the considerable concentration of the urine secreted at the commencement of the attack is essentially due to its small amount. This, as you at once notice, agrees excellently with the view maintained by us, which regards the reduction of pressure and velocity in the inflamed glomeruli as the cause of the reduction in the amount of urine secreted. Moreover, with respect to the source of the albumen and formed constituents of the urine, it is not easy in this form of nephritis to have any doubt. By following Posner's method and throwing the kidney into boiling water, the coagulated albumen can be recognised with the greatest certainty between the vascular loops and the capsule; and, besides, it is obviously impossible for the substances referred to to reach the urine except from the glomeruli, since both the epithelium of the urinary tubules and the interstitial tissues are intact. How greatly the increased permeability of the glomeruli, due to the inflammation, favours the abundant transudation of albumen and blood-corpuscles has already been pointed out. These kidneys, however, are of special value as throwing light on the origin of the casts, at least of the hyaline casts. For precisely as in mechanical hyperæmia, the integrity of the epithelium of the tubules excludes every notion that it is concerned in the origin of the casts. Whether the swollen and perhaps desquamated epithelium of the glomeruli takes part through coagulation in the formation of the casts, is another question; the possibility should not, of course, be rejected off-hand, and must be reserved for further investigation to decide. Till then, however, we may unhesitatingly maintain that the hyaline casts consist of coagulated material, which has been deposited in the tubuli uriniferi from the transuded albumen, under the influence, and with the co-operation of, colourless blood-corpuscles, similarly transuded.

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* Lassar, 'Virch. A.,' lxxii, p. 132.

However sharply characterised, according to the foregoing description, this form of nephritis confined almost exclusively to the glomeruli may be, it is easy to see that it will only rarely be the subject of clinical observation, and still more rarely of anatomical examination. For the exciter of inflammation will, as a rule, affect not only the glomeruli through which it is excreted, but the *epithelium of the urinary tubules* with which it comes into contact. It would not be inconceivable *per se* that some noxæ, which do not affect the glomeruli and their epithelium during their passage, should damage the cells of the tubuli contorti; while for those who regard the participation of the tubular epithelium in the excretion of many substances as proved, this is no longer a possibility but an incontrovertible fact. Many writers are, in fact, convinced that they have succeeded in experimentally producing through the blood severe alterations of the urinary tubules without inflicting any injury on the glomeruli. Kabierske* found that after the introduction of chromic salts under the skin of rabbits, the epithelium of the convoluted tubes was converted for longer or shorter distances into a mass of partly granular, partly glistening, flaky, or more homogeneous substance, containing no nuclei, while the nuclei of vessels of the glomeruli as well as of the epithelium lining the tubuli recti were in an excellent state of preservation. A precisely similar coagulation-necrosis of the epithelium of the convoluted tubules was observed by Browicz in the kidneys of rabbits after poisoning by cantharides, and by R. Cohn† after the subcutaneous application of aloin. Further, Lassar‡ found that when petroleum is repeatedly poured over, or rubbed into the skin of, rabbits there is developed a flaky and granular degeneration of certain areas of the epithelium of the tubuli contorti, which fail to stain, without any noticeable changes in the glomeruli and remaining vascular apparatus. Lastly, Litten§ has demonstrated, in an interesting investigation, that in the rabbit ligature of the renal artery for from an hour and a half to two hours causes coagulation-necrosis of the greater part of the epithelium of the convoluted tubes, on the re-establishment of the circulation, while he at first failed to find any simultaneous alteration of the glomeruli. The coagulation-necrosis so produced is distinguished from the chromic and other forms by its great tendency to subsequent calcification. But however well these results agree with one another, and though I am not disposed to raise objections to their positive side, I have not so far the impression that all alteration of the glomeruli and their epithelial covering has really been excluded by the methods of examination and tests applied. In addition to microscopic examination, which could of course afford no evidence as to a possible increase of permeability, the above-named writers have been content with demonstrating the perviousness of the glomeruli by means of post-mortem artificial or vital self-injection, and with showing that aniline-blue soluble in water does not diffuse through the walls of the glomeruli. That this is an adequate test of function may certainly be disputed, since Herzog proved artificially in our laboratory that this colouring matter also does not diffuse through the walls of vessels altered by inflammation. In fact, Litten* subsequently convinced himself by Posner's method that his former statements as to the integrity and physiological condition of the glomeruli were erroneous.

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* Weigert, 'Virch. A.,' lxxii, p. 254.

† R. Cohn, 'Berl. klin. Wochenschr.,' 1882, No. 5.

‡ Lassar, 'Virch. A.,' lxxvii, p. 157.

§ Litten, 'Zeitschr. f. klin. Med.,' i, Hft. 1.

Still less can any conclusions be drawn from these experiments, with regard to *human nephritis*. For when, in inflammation of the kidney, we find marked alterations of the epithelium of the urinary tubules, it may almost always be shown that neither the Malpighian tufts nor the interstices with the meshwork of capillaries are intact, while in the experiments their condition was expressly stated to be normal by the writers in question. Let us first consider that form of inflammation which is usually briefly called *acute nephritis*, inasmuch as it is comparatively the simplest and certainly the most recent. It is also termed *acute parenchymatous, acute hæmorrhagic,* or *croupous nephritis,* and in it the kidney is always *enlarged* and usually also *hyperæmic*. The surface of the organ is smooth, and as a whole is dark grey-red in colour, yet on closer inspection grey, grey-red, and yellowish spots are found alternating with one another, and between these a larger or smaller number of *punctiform hæmorrhages* are regularly present. Corresponding with these appearances there is likewise found on section *a mottling of the cortical substance,* which is increased in size and its finer marking blurred.

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* Litten, 'Med. Centralbl.,' 1880, No. 9.

Here, too, there are linear and dotted patches of grey, red, and yellow, and also punctiform hæmorrhages, beside which the glomeruli are as a rule clearly discernible. The consistency of the kidneys is somewhat less than normal, and the organs are very full of juice. Yet this description, while applying to the decided majority of cases of acute nephritis, is far from holding true of all. Weigert is perfectly correct in stating that cases occur *in which the hyperæmia is absent.** In these the superficies, and surface of the section are pale, yellowish grey to yellowish white, but in other respects they agree perfectly with the hyperæmic organs—in the enlargement, flabbiness, juiciness, and blurring of the cortical markings; nor are the punctiform hæmorrhages absent. The medullary substance is bluish red in colour, though of a paler shade than in the hyperæmic kidneys.

As regards the microscopical appearances of these kidneys, it is usually said that *the interstices of the cortex are enlarged and infiltrated with round cells.* But if by this statement we are to understand that the interstices *everywhere* present these changes, it is decidedly incorrect. For many portions of these kidneys may be found with their interstitial tissue perfectly normal as regards amount and richness in nuclei, and in consequence vividly contrasting with the interstices of the vicinity, which are actually widened and infiltrated by numbers of lymphoid cells; hence, however numerous these latter areas, the interstitial affection is without exception a *focal* one. Within these foci you will always find evident alterations of the *epithelium of the urinary tubules.* Their cells are converted into lumpy, glistening, amorphous masses, or they appear as if broken and eroded towards the lumen; occasionally they are altogether absent and their place taken by colourless or red blood-corpuscles. The remainder of the epithelium presents no striking pathological changes, if we except certain fat-drops, which are met with here and there in the cells and also in the interstices. In the hyperæmic kidney the fatty degeneration is always trifling; in the pale kidney it is usually more pronounced, although were one to infer from the yellowish-grey colour that extensive fatty degeneration is always present, this would only lead to disappointment. The hæmorrhages which are apparent to the naked eye, are situated in the interstitial tissue, the lumen of the urinary tubules, or the interior of Bowman's capsules in direct proximity to the compressed glomeruli. The intracapsular hæmorrhages undoubtedly point to the involvement of some of the glomeruli, a conclusion which is borne out by other alterations. Such are the thickening and cellular infiltration in the immediate neighbourhood of Bowman's capsules, owing to which the latter are occasionally encompassed by a dense zone crowded with nuclei and cells; further, the swelling and loosening of the glomerular epithelium, in consequence of which the single cells project stud-like into the lumen of the capsule; lastly, the accumulation of round or flattened cells between the tuft and the capsule. This last change is regarded by most writers as the expression of a proliferation of the epithelium, yet it does not appear to me to be established that epithelial cells are really concerned in it. The alterations are not, it is true, equally distributed over all the glomeruli; in acutely inflamed kidneys many are found to be quite free from damage, and no less normal in appearance than are numbers of the interstitial areas and great portions of the urinary tubules.

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* Weigert, 'Volkmann'sche Vortr.,' Nos. 162, 163, contains the most accurate and objective pathologico-anatomical account of Bright's disease with which I am acquainted, and on it my own description is in many particulars based.

It is, however, the ætiology that influences me almost more than these pathologico-anatomical changes in maintaining the participation of the glomeruli in the inflammatory process.[*] In the decided majority of instances acute nephritis is a secondary affection, *i. e.* it appears in the train and certainly under the influence of other diseases which are as a rule, though not always, acute. Of these diseases, I may mention first of all *scarlet fever* and *diphtheria*; further, *relapsing fever*;[†] then *septic* and *pyæmic* processes, *pneumonia*, *typhus*,[‡] *acute rheumatism*; also acute and chronic *valvular endocar-*

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[*] Cf. Wagner, "D. Morbus Brightii," in Ziemssen's 'Handb.,' ix, i, 3 Aufl., 1882, p. 143. *et seq.*

[†] Cf. Obermeyer, 'Virch. A.,' xlvii, p. 161; Ponfick, ibid., lx, p. 153; Wagner, 'D. A. f. klin. Med.,' xxv, p. 529.

[‡] Leyden, 'Ztschr. f. klin. Med.,' iii, Hft. 1; Wagner, 'Morb. Brightii, p. 158.

ditis ;[*] probably, too, *constitutional syphilis,*[†] and other affections. These, you observe, are the same infective processes with which we became acquainted as causes of that nephritis which is confined exclusively to the glomeruli; and because of this, because in these cases the virus of scarlet fever attacks the glomeruli so violently, it appears to me in the highest degree improbable that in so-called acute nephritis the epithelium of the tubules should be damaged and the glomeruli escape. Rather, acute nephritis is, in my opinion, a mere quantitative increase of that form which we have termed *glomerulo-nephritis.* While in the latter the glomeruli alone are affected by the noxa and the epithelium of the tubules escapes, in acute Bright's disease the glomeruli and subsequently the epithelium are more or less seriously involved, and as a result of the implication of the latter the interstices and the capillary network are sympathetically affected. Should it, accordingly, appear to some of you to be of advantage to speak of two stages rather than of two forms of acute nephritis, I can raise no objection *per se ;* yet you will presently hear that the same consideration applies to all the other forms of nephritis, so that so long as different forms continue to be distinguished—and this is certainly to be desired for sake of clearness—we must accept as one of them glomerulo-nephritis with its well-marked clinical and anatomical characters. From this standpoint it will now, however, be quite clear to you why I formerly hesitated to assert the existence of an independent or primary glomerulo-nephritis. An independent acute nephritis is not only positively demonstrated, but is a comparatively common disease. To say nothing of the fact that it has repeatedly been observed after severe poisoning with cantharides, turpentine, and copaiva, and has been produced experimentally by cantharides in rabbits and dogs,[‡] all observers have long been agreed that precisely this acute form of renal inflammation is called forth by sudden *chilling* or *wetting* of the skin, especially when the body is heated and bathed in perspiration. True, we are at present quite ignorant of the causal connection between the chilling of the skin and the nephritis, chiefly no doubt because the question has not hitherto been successfully grappled with by experimental means. The albuminuria setting in in rabbits after varnishing of the skin does not depend on nephritis; and while decided lesions of the kidneys follow inunction with various oils, their occurrence, as Lassar[*] has recently shown, is to be attributed solely to the fact that these oils, after being absorbed through the skin, damage the tissues of the kidneys during their excretion. It is perhaps more to the point to recall the observations repeatedly made that an acute nephritis occurs in the train of tedious *pustular and eczematous affections of the skin*, as well as of *pemphigus* and chronic cutaneous ulcers. Salvioli[†] has indeed succeeded in artificially producing this form of nephritis in dogs by successively painting different portions of the skin with croton oil so as to keep up for weeks a *pustular eczema*. Now, I am not, it is true, disposed to see anything more than a very remote analogy between these true cutaneous inflammatory affections and the process taking place on chilling of the skin; but even though, as we readily admit, the actual factor by which the chill proves dangerous to the kidneys is unknown, it would be over-sceptical to deny the force of observations such, for example, as that communicated by Bartels.[‡] When nephritis develops during pregnancy it appears to me to be mostly of this acute form—to judge at least from the recorded descriptions,[§] which unfortunately I am not in a position to verify. In the bodies examined by me of women who died of eclampsia, with oliguria, hæmaturia, and albuminuria, I have not, as I recently stated, discovered unmistakable signs of inflammation. Moreover, we do not know the agent on which the nephritis of pregnancy depends. But if the clinical and anatomical features of these primary forms of nephritis are precisely the same as occur in the secondary, after scarlet fever, &c., we may fairly conclude that they arise in the same way, *i. e.* that the unknown cause first affects the glomeruli and afterwards the epithelium. But if this be so, we may theoretically assume the existence of an independent glomerulo-nephritis as a kind of first stage in these cases also; though this conclusion is unsupported by anatomical evidence, because, it would appear, the acute nephritis does not in this stage destroy life.

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[*] Cf. Klebs, 'A. f. exper. Patholog.,' iv, p. 427, *et seq.;* Bamberger, 'Volkm. Vortr.,' No. 173; Wagner, 'D. A. f. klin. Med.,' xxv, p. 529.

[†] Wagner, 'D. A. f. klin. Med.,' xxviii, p. 94.

[‡] Cornil, 'Compt. rend.,' xc, p. 536; 'Soc. de [illegible] Jan. 31st, 1880; P. Bos, 'Overdiffu[illegible],' Inaug.-Disser[illegible]; Stüler, 'D. Ztschr. f. Chir.,'

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[*] R. Cohn, 'Berl. klin. Wochenschr.,' 1882, No. 5.

[†] Wagner, ibid., p. 180; Salvioli, 'Arch. p. l. scienze med.,' iii, No. 23.

[‡] Cf. Frerichs, l. c., p. 150; Bartels, 'Handb.,' p. 226; Wagner, 'Morb. Brightii,' p 185.

[§] Cf. Litzmann, 'Deutsch. Klinik,' 1852, Nos. 19 to 31; 1855, Nos. 29, 30. Cf. Leyden, 'Ztschr. f. klin. Med.,' ii, p. 173, who is just as little convinced as I am of the inflammatory nature of the renal affection of pregnancy.

The view of acute Bright's disease just expounded, according to which it is a glomerulo-nephritis intensified by the implication of the epithelium of the urinary tubules and the interstitial tissues, greatly simplifies the understanding of the functional disturbance. For it follows therefrom that the urine must possess all those peculiarities *which an inflammatory alteration of the glomeruli would produce.* As a matter of fact, while the process is at its height the urine is *scanty,* and in very bad cases may be completely suppressed; its *specific gravity is high,* its reaction *acid,* while in colour it varies from a *reddish yellow* to a deep *blood-red;* it always contains considerable quantities of *albumen,* and even when passed is *cloudy,* owing to the presence of numerous *red* and *colourless blood-corpuscles* and other *corpuscular masses,* which when the urine is let stand accumulate as sediment. On more closely examining this sediment, it is found to contain —besides colourless and red corpuscles, from some of which the colouring matter is extracted—numerous long and short, narrow and wide *hyaline* casts, as well as some reddish-yellow ones, the latter more especially if the urine is markedly blood-coloured. In addition there is present a larger or smaller number of morphotic elements, which are rarely and only exceptionally met with in the urine of glomerulo-nephritis. These are single *renal epithelial cells* and short and long *epithelial casts, i. e.* fragments of tubes, consisting of epithelial cells which have been loosened *en masse* from the membrana propria and washed away by the urine; the cells in question retain their normal habitus or contain fat-drops; and, lastly, we find *granular* casts. It is unnecessary to say that all these casts may be occupied by blood-corpuscles or urates.

If we now consider the pathologico-anatomical differences between acute Bright's disease and glomerulo-nephritis in relation to the condition of the urine just described, it is natural to connect the epithelial and granular casts with the alterations of the epithelium of the tubuli uriniferi. As for the epithelial casts, this connection cannot reasonably be doubted; and the view, which has lately been repeatedly urged, that the granular casts also consist of material derived from the tubular epithelium has unquestionably much to support it. Mortification of the epithelial cells over a larger or smaller area by the noxæ passing into the urine is not only easily intelligible but directly demonstrated by the microscopical appearances; in the urinary tubules, however, if anywhere, there is no lack of lymph circulating around and through the epithelial cells, or of colourless corpuscles, by which the epithelial elements might be converted into coagulated material. But if this interpretation be correct the process engaging our attention has an unmistakable analogy to *croup* of the mucous membranes, where the epithelium which is not shed undergoes coagulation-necrosis. The term "croupous nephritis" is consequently justified in an almost unexpected fashion; and not only so, but this view opens up a new and, I think, significant perspective. For just as in croup of a mucous membrane, when after death of the epithelium the fluid exuded from the vessels of the stroma appears on the free surface and there takes part in the formation of the fibrinous pseudo-membrane, do not—we may inquire in the present instance—colourless corpuscles and coagulable albuminous transudation pass from the surrounding capillary network into the interior of the tubules, and thus contribute not only to the albuminuria but to the production of hyaline "*fibrinous casts*"? It is in this way, in fact, that the writers above named explain the albuminuria and casts which are invariably present in poisoning with chromic salts and petroleum; and Weigert* also considers this hypothesis the more probable, as a specially abundant albuminuria is very frequently associated with a specially extensive loss of epithelium. We also shall, I think, willingly adopt this possibility, although, as I need hardly repeat, we distinctly reject the notion that the processes takin [illegible] urinary tubules and surrounding capillaries constitute the only source of the albumen and morphotic elements in acute inflammation of the kidney. An extensive loss of epithelium signifies at bottom simply a *severe* inflammation, and since very many glomeruli will then be very markedly affected, we may without violence refer the unusually profuse excretion of albumen to this cause also.

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* Weigert, 'Volkmann'sche Vortr.,' No. [illegible]

Though a great part of the history of acute nephritis is hypothetical and requires to be cleared up, we have always in such cases to deal with true inflammations, called forth by a definite agent or accident, often of unknown nature, the resulting affection running the course usually followed by acute inflammations. Acute Bright's disease either causes death in a short time if the functional disturbance continues or becomes aggravated, or a gradual improvement sets in after a longer or shorter period. In the latter case, the urine gradually increases in volume and consequently becomes paler and of lower specific gravity; the albuminous contents grow less and less, while the sediment constantly diminishes, till finally the amount and constitution of the urine are again perfectly normal. This course of events is quite familiar to us, as observed often enough, *mutatis mutandis*, in the true inflammations of all kinds of organs, and it were greatly to be wished that the intimate conditions of the remaining forms of nephritis were equally intelligible. The characteristic feature of these forms, serving at any rate to sharply distinguish them from those already discussed, is their *chronicity*. Moreover, they are wont to set in as exquisitely chronic inflammations and to run a chronic course; and only in exceptional cases does the commencement of the disease date from an acute nephritis after scarlet fever or the like. In the latter event, it is certainly conceivable that the inflammatory alteration of the glomeruli and tubular epithelium, brought about by the virus of scarlet fever, was of such severity as to render it impossible for the organism to speedily overcome the disease, though not so severe as to produce a rapidly fatal result. Bright's disease may originate acutely and thus be prolonged for many months, till, after the lapse perhaps of a year, it terminates either in death or recovery.

In the great majority of chronic renal inflammations, however, no such assumption can be entertained, because, as already stated, their origin and course is so insidious that it is not possible, as a rule, to fix the commencement of the disease. In order to explain these forms, we are compelled, so far as I see, to assume *either the continued presence in the organism or kidneys of certain exciters of inflammation*, or to believe *that definite injurious influences*, which need not perhaps in themselves be specially intense, *are very frequently repeated*. These two categories do, in fact, include the principal factors, which have long been recognised as causes of chronic renal inflammation. On the one hand, we have *gout*, *malaria*, and *constitutional syphilis;* and on the other, chronic *lead-poisoning*, the frequent consumption of *alcoholic* drinks, and repeated *chilling* and *wetting of the entire skin*, or of parts of it, *e.g.* the feet. Our judgment of these important questions is unfortunately hampered by a variety of circumstances. One great defect which deprives the numerous statistical conclusions of much of their value is the failure to pay sufficient attention to *amyloid disease* of the kidneys, with regard to which you will presently hear how it influences the constitution and function of the organs. It is impossible now to say how many cases of chronic nephritis, stated to have arisen on a tubercular or syphilitic basis, or under the influence of malaria, would remain, were the examples of amyloid disease discarded. Moreover, the habitual indulgence in an excess of alcoholic drinks is so widely prevalent, especially amongst the inhabitants of large towns, that too much importance should not be attached to the frequent occurrence of chronic Bright's disease in drinkers; and at any rate it is certain that while chronic gastritis, clouding of the pia, or hepatic changes are found in the great majority of inveterate drunkards, their kidneys are mostly in an excellent condition, being large, firm, and supplied with an abundance of blood. Of the morbid conditions of the organism which there is a disposition to place in causal connection with chronic nephritis, there accordingly remains only gout, and of the frequently recurring noxæ, besides lead poisoning, only the chilling of the skin. But unfortunately these fact[illegible]ever great we may estimate their importance, [illegible]ng the cases of chronic nephritis which actually come under observation; and even if we have recourse to extensive and severe *sclerosis of the renal arteries* for the explanation of a number of exquisitely chronic examples, there yet remain not a few instances in which we are unable to point to any palpable cause.

That these chronic renal affections are really actual and genuine examples of nephritis we are most unmistakably taught by the anatomical appearances. Two types of chronic Bright's disease have been distinguished, mainly by English writers, and amongst German pathologists Bartels has most unreservedly accepted their conclusions. These types are not only very different when fully developed, but are asserted to have nothing in common in their genesis; they are, namely, the "*large white kidney*," called by Bartels "chronic parenchymatous nephritis," and "*the red contracted kidney*," corresponding to our *contracted* or *granular* kidney. Yet Bartels and his predecessors, in carrying out this sharp distinction through all the clinical details, have failed to guard against the inclusion of amyloid disease of the kidney with pure and uncomplicated chronic nephritis; and thus it has come about that the picture painted by Bartels* of his chronic parenchymatous nephritis applies in all essentials to amyloid nephritis and only exceptionally to pure Bright's disease. Chronic nephritis does really present itself post mortem in different forms; and were it desirable to set up a special type for each, it would be easy to construct, not two, but five or six or more, even if we were only to take into account the considerable differences in size, colour, consistence, condition of the surface, &c. Yet these striking naked-eye differences are not represented by equally great microscopical ones; rather the differences with which we have to deal, as Weigert† rightly recognised and clearly stated, are not so much fundamental as gradual ones: the granular kidney simply represents a much more advanced stage of the disease than the large chronically inflamed kidney. Moreover, the sharp distinction and contrast drawn between a "parenchymatous" and an "interstitial" nephritis does not, as you will shortly hear, bear the light of an unprejudiced microscopic investigation; and thus we again approach, in the revolution of science, the standpoint taken up by Bright in his celebrated researches, and subsequently by Reinhardt and Frerichs, namely, *the unity of true nephritis.* I wish, however, to warn you most emphatically against so far following the view of the writers just named, as to regard the different forms of nephritis as different following stages of the inflammatory process. In the case of glomerulo-nephritis and acute Bright's disease, this, as I remind you, would certainly be admissible, and it may also occasionally happen that an undoubted case of acute nephritis becomes chronic and perhaps terminates in contraction. This is not, however, the usual course. The rule is that persons suffering from acute Bright's disease either die or recover; while the very great majority of chronic renal inflammations, as has already been stated repeatedly, run from the very commencement an exquisitely insidious course, without any acute stage whatever. And with reference to the chronic forms also, it would be quite erroneous to suppose that granular atrophy is always preceded by a stage of enlargement; if such cases occur at all, they are certainly exceptional. It is true indeed that if we find granular kidneys in the dead body, we must date the commencement of the nephritis further back than if we meet these organs in a condition of morbid enlargement. But this does not at all justify us in concluding that the kidneys must have been enlarged before they atrophied. On the contrary, one may perhaps formulate the proposition in this way, and say that the process only then leads to complete granular atrophy when it runs such a slow and insidious course that the kidneys never undergo an actual increase of volume.

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* Bartels, l. c., p. 290, *et seq.*

† Weigert, 'Volkmann'sche Vortr.,' Nos. 162, 163.

Let us now turn to the pathologico-anatomical details of chronic Bright's disease. In the bodies of individuals who have shown symptoms of an inflammatory renal affection, as evidenced by the state of the urine and other conditions, for a period varying from six months to a year or perhaps somewhat longer, we occasionally find the kidneys in the following condition. The organs are more or less *swollen* and have *a smooth* surface which as a whole is a dark greyish red in colour, but is mottled with yellow or yellowish-white spots;

the surface of the section is similarly mottled, and the cortical markings are blurred: in fact the organs are distinguished from the acutely inflamed kidneys only by their somewhat greater *firmness*, for the hæmorrhagic points and stripes are also present. More frequently, however, we meet under these circumstances with kidneys which perfectly agree with those just described, except that instead of being red or greyish red, their cortex and therefore surface are *pale—yellowish* or *yellowish white*—while the pyramids are sharply marked off from the cortex by their bluish-red colour. These two forms, termed by Weigert* *chronic hæmorrhagic nephritis*, are distinguished from each other on microscopic examination only by the more marked *fatty degeneration of the epithelium* and of the interstitial tissues in the pale kidneys, except that the blood-contents are of course unequal; but all the other changes, which are functionally much more important, are precisely similar in both. These alterations, however—to refer to this point at once—are never diffused over the entire organ, but occur in distinct patches, though many of the larger patches come into contact by their prolongations. In the foci, no portion of the renal tissue escapes the disease. Some foci select the *glomeruli*, where we find intra-capsular hæmorrhages, loosening of the epithelium and proliferation of the nuclei of the capsules; in some glomeruli there are further alterations, namely their compression and conversion into spherical masses of connective-tissue with few nuclei; while around the capsules more or less large masses of unmistakable connective tissue, mostly abounding in nuclei, are found. The foci conditioned by *diseased urinary tubules* are, however, larger and more numerous. Here we have not to do so much with fatty degeneration of the epithelium, which is much more marked outside the foci, as with atrophy and, most frequently, complete destruction, *loss of the epithelium*. The urinary tubules are considerably narrowed in consequence, and around them the normal interstitial tissue is replaced by more or less thick masses, which in many spots are closely packed with round cells, but in many others consist of *fibrillated connective-tissue poor in cells and nuclei*. Here and there the walls of some of the *smaller arteries* show slight degrees of that *sclerotic thickening,* which they are so prone to develop when participating in the chronic inflammatory processes taking place in their vicinity. As already stated, these changes are all equally present in the red and pale kidneys, and if we regard them as the essential pathologico-anatomical appearances, I cannot see why the two forms should be separated. There can be no doubt, in fact, that the more pronounced fatty degeneration is solely the result of the reduced supply of arterial blood; and this reduction is comprehensible enough on reflecting how great are the resistances interpolated by the inflammatory process even at the commencement of the renal vascular system. The greater the number of glomeruli affected and the more severe the circulatory disturbance in them, the more will the retardation of the stream prevail over the hyperæmia, and the less will be the blood-supply to the entire organ.

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* Weigert, 'Virch. A.,' lxx, p. 500; 'Volkm. Vortr.,' p. 6, *et seq.*

You now perceive how correct I was in stating that the attempt to draw a fundamental distinction between a parenchymatous and an interstitial renal inflammation cannot stand the test of a microscopic examination. Nothing of course is easier than to hand a person a microscopic section prepared from such a kidney with the interstices much altered, together with another showing normal epithelium. But the opposite is equally easy, and as a matter of fact *the alterations of the epithelium and of the interstices are always found simultaneously* in this form of chronic nephritis also. You will probably be still more interested in learning that the organ, in spite of its general and often not inconsiderable increase of volume, presents defects, or—to employ the *terminus technicus* made use of more especially in the case of the kidney—*contraction-processes.* These involve both the glomeruli and tubules, and are only compensated, or even over-compensated, by the increased volume of the interstitial tissues. This fact is the more worthy of notice as it at the same time supplies the key to the understanding of the *still more chronic* forms of nephritis. For when the renal affection has lasted a still longer time than in the form just discussed, we meet post mortem with a novel appearance, that of *uneven* or, as they are called, *granular* spots on the surface of the kidney. It is as a rule characteristic of these that the depressions are distinctly red while the projections are grey or yellowish grey—a sure sign that in the depressions the tubules have completely disappeared, leaving only a vascular connective tissue, while the prominences contain more or less well-preserved parenchyma. The number of these granulations increases the longer the disease lasts, and in making the autopsy of an individual who has suffered for years from nephritis, you may be certain of finding those *small, usually red or greyish-red, more rarely pale kidneys, of leathery, tough consistence,* with a considerably *diminished cortex* and *rough surface* from which the typical description of the *granular* or *contracted* kidney has been drawn. The gradual reduction in size of the kidneys in consequence of a widely distributed process such as this is explained simply enough by the well-known tendency of newly formed connective tissue to retraction and shrinking, which go on unopposed after destruction of the tubules. The regularly occurring thickening of the walls of the small arteries in the granular kidney is an appearance found in the analogous chronic inflammatory processes in all organs. As for the other details with regard to these contracted kidneys, and in particular the description of the mostly microscopic *cysts,* and of their origin through occlusion of Bowman's capsules or obstruction of urinary tubules, these may be left to pathological anatomy and histology.

But how do the kidneys perform their function when in a condition of chronic inflammation? In that form of chronic nephritis in which all the anatomical alterations found in acute inflammation of the kidneys are present, we shall expect the urine to resemble in all essential characters that secreted in acute Bright's disease. The urine of these chronically inflamed kidneys does in fact contain *albumen* at all times, and generally in considerable amount; it throws down a *copious sediment,* containing a variable quantity of *red,* but always large numbers of *colourless corpuscles;* numerous *casts* are constantly present, and often every variety, epithelial and hyaline, granular and glistening, of every length and thickness; and in addition some *granular corpuscles* and *fatty detritus* are found. In one respect, however, the urine of this chronic nephritis differs very markedly from that of acute inflammation, namely, in *volume;* in the chronic cases the amount of urine is never so reduced as in the acute ones, but usually *keeps at about the normal standard*, occasionally exceeding it a little, or falling short of it, if at all, only to a trifling extent. Owing to its greater volume, the urine in these cases is not brownish red or blood-red, but *pale* or *dull yellow*, and its *specific gravity*, instead of being raised, is abnormally *reduced*. The more the nephritis assumes an insidious character and the more chronic the course of the process, *the more abundant, pale, and light will be the urine, while the albuminous contents and the sediment become proportionately less;* and by the granular kidneys finally there is secreted a very considerable *quantity*—often two or three times the usual amount—*of light yellow*, or rather greenish-yellow, almost perfectly *clear urine of very low specific gravity* (1006—1008—1010), which as a rule contains only minute quantities of albumen, and is sometimes non-albuminous, while its formed elements consist of a few of both kinds of blood-corpuscles with an odd hyaline or granular cast. However intelligible it is that with such an extremely insidious course, where the essentially inflammatory changes are not at any time extreme or widely distributed, the albuminuria and excretion of formed elements should never be anything more than trifling, it is more difficult to explain the large quantity of urine. For it is natural to suppose that it would be diminished so long as the high albuminous contents and abundant sediment indicate the presence of foci of active inflammation, while a decrease of the urinary secretion would appear to be equally naturally the result of the destruction and imperviousness of numbers of the glomeruli and tubules. And indeed the large volume of the urine cannot be explained from the condition of the kidneys themselves. Rather it is the effect of occurrences which afford some of the most striking evidences of the great regulative capabilities of our organism, namely, *the rise of arterial pressure and the cardiac hypertrophy which develop under the influence of the chronic renal inflammation.*

That chronic nephritis is very frequently complicated by *hypertrophy of the heart*, chiefly of *the left ventricle*, has since Bright's first communications on the subject been confirmed times without number, both at the sick-bed and in the post-mortem room; and it is not the fact itself but the nature of the connection that still continues to give rise to differences of opinion.* No one has devoted more careful and continued attention to this question than Traube. He was the first to formulate a mechanical theory of the dependence of the cardiac hypertrophy on the nephritis.† According to him the contracted kidney causes an increase of the mean tension in the aortic system, and so offers abnormal resistances to the heart, by "bringing about a diminution in the quantity of fluid withdrawn from the aortic system for the formation of the urinary secretion," and by "diminishing the quantity of blood flowing in a given time from the aortic into the venous system." He has perhaps done still greater service in having followed with the greatest accuracy during life the alterations in the circulation which are developed in the course of nephritis, and having determined their clinical signs. Traube has recorded his experience on this point in several essays, and while he at first expressed himself with some reserve, as years passed on he became more and more convinced by his increased material that symptoms connected with the circulatory apparatus may set in in youthful and otherwise healthy individuals as early as the *first few weeks* in severe nephritis, which indicate in a most unmistakable way an *increase of tension in the aortic system.*‡ These signs are abnormal resistance of the radial arteries and of the cardiac impulse, together with loud, high, and ringing diastolic aortic and carotid sounds; and to these there is quickly added the *increased volume of the heart,* so that Traube was able to determine the presence of cardiac hypertrophy as early as *four weeks* after the commencement of the nephritis. In children more especially a short time appears to suffice for its development; at least Friedländer found a marked enlargement of the heart during an epidemic of scarlet fever in almost all the children who died of an acute nephritis scarlatinosa.§ In adults, on the contrary, such a rapid development is rare; a much longer time is required, as a rule, before the higher degrees of arterial rise of pressure and cardiac hypertrophy can be detected. These are, consequently, wont to be more pronounced the more chronic the course of the nephritis; but in the uncomplicated granular atrophy of strong individuals they form such constant and characteristic phenomena that experienced clinicians can diagnose the contracted kidneys solely from the pulse, *i. e.* from the high tension of the artery in all other respects normal.

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* A thoroughly complete literary historical compilation of the numerous discussions dealing with this question is given by Zander, 'Ztschr. f. klin. Med.,' iv, Hft. 1 and 2.

† Traube, 'Ueber d. Zusammenhang v. Herz.- und Nierenkrankheiten,' Berlin, 1856; 'Ges. Abhandl.,' ii, p. 290.

‡ Traube, 'Ges. Abhandl.,' iii, pp. 235, 427, *et seq.* In addition numerous essays on nephritis in Bd. ii and iii.

§ Friedländer, 'Arch. f. Phys.,' 1881, p. 168.

But though these facts render it very probable that there is a direct relationship of dependence between chronic nephritis and hypertrophy of the heart, there have always been pathologists who denied this causal connection, and the last few years more especially have increased their number somewhat. The majority of the opponents of the view hold that the attempted explanations of this dependence have not been successful, and confine themselves to denying it because it is unintelligible; some, however, have gone further, and have sought to substitute another theory for that called in question by them. Of these we must first mention Gull and Sutton,* who look upon the cardiac and renal affections as *co-ordinated, and due to a peculiar degeneration of the small arteries* of all parts of the body, for which they have proposed the name, *arterio-capillary fibrosis.* Strange to say, these English writers, if I correctly understand them, in dealing with the renal affection always refer only to the contracted kidneys, so that their explanation, even if correct, could not apply to the large inflamed kidneys, in which, however, cardiac hypertrophy also occurs. As regards the facts underlying their observations I wish to make a few remarks. According to our experience, there are kidneys which have atrophied and become contracted in consequence of an extreme sclerosis of their middle-sized and smaller arteries; they are not uncommonly found in persons advanced in life, and I have often seen them in syphilis; and precisely in this form the cardiac hypertrophy is, as a rule, absent, owing to the senile or syphilitic marasmus. On the other hand, the smaller renal arteries often present thickenings of their walls in the true granular atrophy of younger individuals; but this, as already mentioned, is not a primary alteration; it is simply the chronic endarteritis obliterans, so called by C. Friedländer, which so frequently becomes associated with the chronic interstitial inflammations of all organs.* The statements of Gull and Sutton as to the existence of a *general* arterial disease in these cases appear still less tenable. In an extensive examination of appropriate cases, Ewald† failed to detect either a degeneration or any signs of chronic inflammation of the small arteries; the only arterial change he claims to have often found in these cardiac hypertrophies is a thickening of the *muscular coat* which he regards as the secondary effect of the hypertrophied heart-muscle. Without entering upon a criticism of Ewald's methods of examination, I wish to remark that according to my experience even this muscular hypertrophy of the arterioles cannot be so frequent as would appear from his statements;‡ at least I have repeatedly failed to find any noteworthy alteration of the walls either of the larger or smaller arteries in most typical cases of contracted kidney and extreme hypertrophy of the heart.

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* Gull and Sutton, 'Med. Chir. Trans.,' 1872

According to a second view, energetically defended by Senator,§ the cardiac hypertrophies occurring in renal inflammation must be carefully distinguished into two kinds, an hypertrophy with dilation—*excentric,* and one without dilation—*simple.* The former is stated to be found chiefly in "chronic parenchymatous nephritis," *i. e.* our chronic hæmorrhagic, enlarged, or at least undiminished, kidneys, and to be here the result of the persistent overloading of the blood with urea—of which more presently; while simple cardiac hypertrophy is said to be mainly observed with contracted kidneys, but depends so little on the renal affection that this is to be regarded rather as a consequence of the heart lesion, probably through implication of the small renal arteries. Now, to say nothing of the many gaps in this argument, or of the fact that the state of contraction of the heart often makes it impossible to form a reliable opinion as to the capacity of the ventricular cavity, the anatomical basis of the theory is incorrect. I have seen, not simply once, but often, the most marked excentric hypertrophy of the heart, amounting even to complete cor bovinum, associated with the most genuine contracted kidneys; and, on the other hand, in chronic hæmorrhagic large kidneys one meets with simple cardiac hypertrophy not merely as often but, according to my recollection, oftener than with the excentric variety. Senator also admits that exceptions to his rule occur, although the importance of his argument is clearly seriously lessened thereby.

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* Cf. Wagner, 'Morb. Brightii,' pp. 93, *et seq.*, 301, *et seq.*

† Ewald, 'Virch. A.,' lxxi, p. 453.

‡ Sotnitschewsky, 'Virch. A.,' lxxxii, p. 209, has arrived at the same conclusion.

§ Senator, ibid., lxxiii, pp. 1, 313.

A third theory has been advanced by Buhl, also within the last few years.* The name of its author is a guarantee that it contains suggestive and fruitful ideas; nevertheless you will willingly dispense with details on learning some of its main propositions. According to Buhl, the cardiac hypertrophy depends on inflammatory fatty degeneration of the musculature or more intense myocarditis. The hypertrophy is set up either directly on the termination of the inflammation, in accordance with the general law that every inflammation is immediately followed by a stage of "over-nutrition;" or there is first developed a dilatation of the cavities of the heart, which is followed by an hypertrophy, inasmuch as the dilated ventricles have to propel a larger quantity of blood. The development of the hypertrophy is further favoured by the fact that the aorta not merely does not participate in the enlargement of the heart, but even becomes narrowed, owing to the decrease in the total amount of blood regularly brought about by the albuminuria and by the digestive disturbances so commonly present; a *relative* narrowness of the aorta sets in, and as a result the hypertrophy of the left ventricle must be still further increased: for the rest, the rise of pressure is only systolic because the arterial valves close. In what way these statements, taken almost verbally from Buhl's communications, are to be reconciled with the conclusions arrived at by us from our study of the pathology of the circulation, this I must leave you to decide for yourselves; to me at least the foundation on which these views rest appears to lie so remote from our own that any attempt at a reconciliation must be fruitless.

* v. Buhl, 'Mittheil. aus d. pathol. Inst. zu München,' 1878, p. 38.

A theory claiming to explain the dependence of the cardiac hypertrophy on the nephritis must above all be in accordance with the facts observed in the patients in question. But it is a fact that *the rise of arterial pressure precedes the enlargement of the heart,* so that no explanation according to which the high tension of the arteries is conditioned solely by the cardiac hypertrophy can be correct. Is it not *per se* very much more probable, as well as consonant with all our knowledge of the circulation, that a healthy heart with undisturbed innervation hypertrophies because it must overcome the abnormal resistance arising from the high arterial tension, rather than that any unknown influence should supply the impulse to the excessive growth? And in spite of Buhl's assertion to the contrary, I can assure you that a large number of the hypertrophied hearts of the nephritic *are* healthy, the endo- and peri-cardium being absolutely intact, the valves delicate, and the myocardium red in colour, without any cicatricial tissue, and mostly, too, without any fatty degeneration. In the second place such a theory must be adapted to explain not only the cardiac hypertrophy occurring in contracted kidney—to which alone the discussion was, owing to an unfortunate misconception, at first confined—but must also serve to elucidate the hypertrophy which makes its appearance in a nephritis running a much shorter course, and which is found post mortem associated with large inflamed kidneys. For the notion that we have here to do, perhaps, with different forms of enlargement of the heart has just been repudiated by us. In the third place, and lastly, the cause of the hypertrophy of the heart must not be sought in a factor which is directly done away with by the hypertrophy, because it would then be impossible to understand why the hypertrophy not only lasts but goes on increasing, at least for a considerable period. Call to mind the cardiac lesions: hypertrophy of the right ventricle cannot render the bicuspid valves again capable of closure, and simply compensates the prejudicial effects of the valvular lesion on the circulation; and did the augmented work of the ventricle actually do away with the valvular defect, there would be no ground whatever for the development of a cardiac hypertrophy.

On now trying whether the theories hitherto formulated satisfy these postulates, we find, in the first place, that there are serious objections to the view according to which the chief weight attaches to the *alteration in the constitution of the blood* brought about by the renal affection. The exact nature of this alteration has not been stated either by Bright who first announced this theory, which we may call the chemical, or by the many pathologists who have adopted it, more especially in England. Ewald* and Senator,† moreover, the most recent writers inclining to this view, confine themselves to the statement that the accumulation of urinary constituents, especially of urea, forms the injurious factor. But as to how this impurity of the blood originates the rise of pressure and cardiac hypertrophy, the writers just mentioned hold different opinions: Ewald believes that the blood overloaded with urea meets with abnormal frictional resistances in the capillaries, and consequently flows more slowly through them; Senator, on the other hand, thinks that the urea accumulated in the blood has the power of directly causing a rise of pressure—an effect which Ustimowitsch and others have actually observed after the injection of a solution of urea into the blood. True, Ewald has not succeeded, in the experiments undertaken by him, in showing his theory to be probable, to say nothing of verifying it; and Senator has overlooked the fact, that to cause a brief and insignificant rise of pressure of about 20 mm. mercury, it is necessary to introduce a quantity of urea which in the same proportion would be regarded as enormous in man, while his assumption becomes still less likely from the circumstance that a second injection of urea fails to cause a rise of pressure after such a rise has been occasioned by the first.‡ Now Israel,§ it is true, has recently reported the successful production of an *hypertrophy of the kidneys* followed by an *hypertrophy of the heart* by continuously administering to young rabbits gradually increasing doses of urea by the mouth; the dose being increased during three to four weeks from two grains *pro die* up to eight grains and later to even twelve grains and more.

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* Ewald, 'Virch. A.,' lxxi, p. 453.

† Ustimowitsch, 'Ber. d. sächs. Ges. d. Wiss.,' M. Phys. Cl., 1870, p. 430.

‡ Israel, 'Virch. A.,' lxxxvi, p. 299.

§ Traube, 'Ueber d. Zusammenhang v. Herz- und Nieren-krankheiten,' Berlin, 1856; 'Ges. Abhandl.," ii, p. 290.

The hypertrophy took place although the animals became *greatly emaciated* and presented various evidences of feebleness. Yet since in judging of the size of the heart he employed a criterion whose unsuitableness has been clearly demonstrated by Zander,* namely the ratio between the weights of $\frac{\text{kidney} + \text{kidney}}{\text{heart}}$, Israel will not think ill of my entertaining some doubt as to whether all the hearts held by him to be hypertrophied actually deserved to be called so; and I must also be excused for doubting whether the cardiac hypertrophy, if really present, need be ascribed to the feeding with urea, the influence of which in producing emaciation and feebleness of the animals was observed by the experimenter himself. Moreover, Israel has not given us a satisfactory explanation of the mechanism by which the overloading of the blood with urinary constituents influences the heart and vascular system so as to produce a rise of pressure. But be the fact as it may, any theory based upon it should still, in my opinion, be rejected, because at best it would apply only to that form of nephritis in which the excretion of solid urinary constituents is for a long period considerably reduced below the normal. Something might be made of the theory in cases where a chronic nephritis is developed from an acute one, and perhaps too in cases of chronic hæmorrhagic inflammation of the kidneys; but it is quite inadequate, as Senator also correctly perceived, for the markedly chronic forms which result in the production of granular kidneys, because these insidious inflammations never lead to a lasting diminution of the excretion of urea, nor, consequently, to a retention of the solid urinary constituents in the blood.

The same objection applies with full force to that part of Traube's theory which regards the *diminution of the volume of the urine* and the simultaneous increase of the volume of the blood as a factor increasing the blood-pressure—although this very line of argument has recently again been adopted and warmly defended by Bamberger.† In markedly chronic nephritis leading to granular atrophy there need be at no time a diminution of the urine worth mentioning; indeed, its volume may permanently exceed the normal on from the day when for the first time a suspicion even of renal disease had arisen: and yet it is precisely in these cases that the most marked hypertrophy of the heart is developed. But if the blood of persons with contracted kidneys and hypertrophied hearts be examined at a time when the state of well-being of the patients is comparatively good, the perfectly normal conditions as regards specific gravity, urea- and water-contents will be found to be preserved, so that Bamberger's idea that the water-balance of the organism is adjusted at a higher level is in point of fact untenable, to say nothing of the theoretic objections to it. Moreover, I need only indicate how little this water-retention theory meets the third of our postulates. But perhaps the weightiest objection to the view is afforded by the evidence brought forward by Lichtheim and myself *that even the strongest hydræmic plethora cannot raise the blood-pressure above the normal values* (cf. Sect. I, Chap. VIII). We need not, of course, discuss the question, in itself debatable, whether an increase of the volume of the blood makes augmented demands on the work of the heart, despite the absence of any rise of arterial pressure. For we have to explain the rise of arterial pressure and not the hypertrophy of the heart; and because this is so, our experiments on hydræmic plethora in my opinion most conclusively overthrow the water-theory.

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* Zander, 'Ztschr. f. klin. Med.,' iv, Hft. 1 and 2.

† Cf. Bamberger, 'Volkm. Vortr.,' No. 173.

Accordingly we have no resource, so far as I see, but to recur to *circulatory disturbance in the kidneys, i. e.* to maintain the correctness of this part of Traube's explanation, although not, as I may at once add, in its original but in modified form. Traube selected as the determining factor that in contracted kidney the amount of blood passing in the unit of time from the aortic into the venous system is diminished, or, in other words, that *abnormal resistances oppose the passage of the blood through the kidney;* and this fact does not need to be specially proved. But to the conclusion that an abnormal rise of pressure in the aortic system must result therefrom, it has been objected with apparent justice that it is impossible to see why a compensation should not somehow be effected here, just as when the resistance is increased in other organs. Now the answer to this question has, I believe, been supplied in our discussions on the effects of local anæmia on the circulation as a whole (vol. i, p. 127, *et seq.*). For we were then able to determine that an abnormal resistance when interpolated anywhere in the arterial system is not followed by a general rise of blood-pressure, if *pari passu* with the increase of resistance in one area there takes place a corresponding decrease of resistance in another, or if—should such compensation fail to occur—a certain quantity of blood, having become superfluous, is removed from the circulation. The former, the compensatory hyperæmia, does certainly take place in the second kidney when only one has become anæmic; but when both kidneys are the seats of lasting local anæmia, there is no organ which could become permanently hyperæmic; while, on the other hand, a portion of the blood would not under these circumstances become "superfluous," unless the blood entering the kidneys were reduced by the amount which would correspond to the resistances on the two sides. Clearly, it is on this point that everything depends: if the kidneys with diminished or obstructed stream-bed are supplied with a proportionately smaller quantity of blood, a rise of general arterial pressure cannot possibly at any time be the result of the impediment; but if, in spite of the latter, the blood-supply to the kidneys remains unchanged, the rise of pressure is inevitable. The amount of blood flowing to the kidneys, however, depends, *cæteris paribus*, on the calibre of the renal arteries—not, of course, of the main trunks and larger branches, which are hardly liable to physiological variations, but of those smaller offsets, whose circular muscular coat is "tonically" contracted, and on which chiefly the vaso-constrictors and dilators exert their influence. But what determines, I ask, the degree at any time of contraction of these small arteries of the kidneys? We know with regard to some glands, and consider ourselves justified in assuming with regard to others, that excitation of their secretory nerves is always attended by a simultaneous excitation of the vaso-dilators. In the kidneys there are no secretory nerves, and, it would appear, no vaso-dilators; yet no one doubts that when a copious secretion of urine is taking place, a large amount of blood flows through the kidneys, and that consequently their small arteries must be dilated. Since, however, much urine is secreted when much water, urea, common salt, or other potential urinary constituent is present in the blood, we formerly believed ourselves correct in assuming that the degree of contraction of the small renal arteries *depends on the amount of such constituents present in the blood.* This has ceased to be a mere hypothetical, though highly plausible, law. For Charles Roy and I* have succeeded in accurately demonstrating by means of the renal plethysmograph that the *introduction of watery solutions of common salt or of urea into the blood* in such small doses as not in any way to influence the general arterial pressure is followed either at once, or after a very brief period of contraction, by *a considerable increase in the volume of the kidney, i.e.* by *a dilatation of the renal arterial channels.* Whether this occurs as the result of a direct influence on the arterial musculature, or by means of nervous agency, need not now be discussed; for the necessary inference in either case is that whether the blood-stream through or beyond the glomeruli is impeded or not, the calibre of the small renal arteries, and hence the amount of blood entering the kidneys, *will remain as before, provided the quantity of potential urinary constituents in the blood continues unchanged.* The increase of arterial tension accordingly sets in as the inevitable consequence of the abnormal resistances interpolated in the renal circulation beyond the small arteries; and in this conclusion we cannot, in my opinion, be shaken by the fact that ligature of both a. renales themselves does not raise the general arterial pressure. This fact, which for the rest plainly tells against the possibility of a rise of pressure through an accumulation of solid urinary constituents in the blood, is sufficiently intelligible from our point of view. For the decisive factor is the disproportion between the unaltered supply of blood to, and the abnormal resistances in, the kidneys; and who would be disposed to doubt that, after ligature of the a. renalis or its equivalent, extirpation of the kidney, our organism, if life was maintained, would simply rid itself of that quantity of blood which it possessed in excess of the requirements of the remaining organs?

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* A short *résumé* of the experiments has been given by Roy in the 'Proceedings of the Cambridge Philosophical Society,' May 23rd, 1881; the full communication will shortly appear in 'Virchow's Archiv.'

From the considerations just dwelt upon it follows that an hypertrophy of the heart must develop when (1) *the blood-stream in both kidneys beyond the small renal arteries*, or at any rate throughout a great part of their vascular system, *is opposed by abnormal resistances*, and (2) the general condition of the individual and in particular his diet is such that *at least approximately the normal amount of potential urinary constituents is produced.* You will please notice that I formulate this law generally, and not merely with reference to nephritis; if correct, it must evidently hold good for other than inflammatory increase of resistance. The most desirable thing no doubt would be, if possible, to prove it by experimental means, and you may therefore imagine with what pleasure I hailed the appearance lately of some investigations which seemed to supply this desideratum. The author of one of them, Lewinski,* attempted to bring about the atrophy of both the kidneys by narrowing first one and then the second a. renalis, and believes that out of twenty-five experiments he has five times succeeded in producing "an idiopathic cardiac hypertrophy without dilatation;" yet the detailed account of his experiments will hardly have the effect of convincing the unprejudiced reader of the correctness of his belief. For in none of the five experiments has Lewinski succeeded in causing the desired atrophy of both kidneys; at most one kidney, and not even this in all cases, reacted to the operation by complete atrophy; and though in several instances the second kidney underwent a compensatory enlargement he claims that in spite of this a cardiac hypertrophy, often extreme, was the result, and that it sometimes developed in from twelve to fifteen days! In view of the innumerable pathologico-anatomical, experimental, and recent surgical experiences as to the complete insignificance of the absence of one kidney to the circulation, it certainly requires an astonishing amount of *naïveté* to entertain one's fellow-scientists with such tales, a *naïveté* which is perhaps only surpassed by that which accepts Lewinski's results in all good faith, without a word of criticism.

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* Lewinski, 'Ztschr. f. klin. Med.,' i, p. 561.

Grawitz and Israel* adopted another mode of procedure, and produced a more or less extreme atrophy of one kidney by applying in the well-known way a ligature to the a. renalis for from an hour and a half to two hours. When the animals operated on were young, there was developed in a short time such a complete compensatory hypertrophy of the second kidney that the operation produced no effect on the vascular system or general condition; in older rabbits, however, the enlargement of the second kidney failed to set in or was inadequate, and in its stead an hypertrophy of the heart took place. Unfortunately, the paper contains some other statements which do not tend to increase one's confidence in the results at which the above-named writers have arrived. In the animals experimented on they also measured the arterial pressure, and, despite the cardiac hypertrophy, failed to find the slightest rise of tension; on the other hand, they claim to have detected, by measuring the rate of the blood-stream in each of these animals, an increase of velocity, provided the enlarged heart was not secondarily diseased. Now it is evident that these results cannot all be correct, since in part they directly contradict each other. If the blood be unaltered in constitution—and no change is mentioned by the writers—the velocity of the flow depends upon the difference of tensions between the arterial and venous systems, so that no acceleration of the blood-stream can occur unless the arterial pressure is raised. And since, as you are aware, every cardiac hypertrophy necessarily augments the arterial tension, an individual in whom the tension is permanently normal cannot be suffering from cardiac hypertrophy, and *vice versâ*. Urged by these remarks of mine, one of the two writers, Israel,† a young man who imagines that he adds to the cogency of his arguments by speaking disrespectfully of his critics—has again measured the arterial pressure in a number of the animals experimented upon, and has now actually found a rise of blood-pressure of from 3 to 6 mm. mercury—a statement which might be taken as a joke, did not the author himself add that these changes are "quite within the normal limits." But when Israel by a careful position in a measure excuses the absence of a rise of pressure, and seeks to show on the contrary that a rise could not possibly occur under the conditions presented by nephritis and atrophy of the kidney, he has evidently forgotten that in human contracted kidney the increased arterial tension forms one of the most constant and striking symptoms. But you will gladly dispense with the details of that remarkable exposition, on learning that a repetition of the experiments of Grawitz and Israel, carried out by Zander* in Neumann's laboratory on a large number of animals, has not confirmed their results; neither after extirpation of the kidneys nor the production of renal atrophy by temporarily occluding the a. renalis was there ever any enlargement of the heart, although the animals remained alive till seven and a half months after the operation. But though it must accordingly be confessed that the dependence of the cardiac hypertrophy on the renal affection has not so far been experimentally proved, there is fortunately no dearth of pathological experiences which have almost the value of an experiment. In *hydronephrotic atrophy*, which will presently be more minutely discussed, very considerable resistances are interpolated in the renal circulation, and we should therefore expect that an hypertrophy of the heart should develop in the course of time in persons with bilateral hydronephrosis, provided that their state of nutrition is good. In the great majority of cases of bilateral hydronephrosis, *e.g.* in all those occasioned by tumours of the pelvic organs, this condition is not, it is true, satisfied, but in bilateral hydronephrosis otherwise conditioned I have repeatedly observed a moderate degree of cardiac hypertrophy, and marked degrees of it have frequently come under my notice. Thus, the museum of the Pathological Institute in Breslau contains specimens removed from a boy, aged eleven, in whom the orifices of both ureters were occluded by a very large vesical calculus: the resulting bilateral hydronephrosis was accompanied by an enormous hypertrophy of the left heart. I also saw a second very striking case in Breslau, that of a boy, aged eight, with the most advanced rachitis, who for a long time lay in the surgical wards. Owing to the extreme narrowing of the pelvis, an enormous dilatation of the rectum and sigmoid flexure had developed, and the narrow pelvic cavity was in consequence so encroached upon as greatly to interfere with the escape of the urine into the bladder, and thus gradually to bring about enormous dilatation of both ureters and hydronephrotic atrophy of the kidneys. All the time the boy was in hospital his pulse was very tense, while the autopsy revealed a very considerable hypertrophy of the left ventricle; with this was probably connected the polyuria occurring during the last weeks of life, which was so considerable as to suggest the idea of diabetes insipidus. An exquisite case of left cardiac hypertrophy, without valvular lesion, in conjunction with extreme hydronephrosis had already been observed by Friedreich.* Moreover, the literature† contains many statements with regard to cystic kidneys where the post-mortem examination revealed considerable hypertrophy of the left ventricle. Observations such as these leave no room for doubt, I think, as to the dependence of the cardiac hypertrophy on renal affections, in which considerable resistances are permanently present in the vascular system of the kidneys.

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* Grawitz und Israel, 'Virch. A

† Israel, 'Virch. A.,'

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* Zander, 'Ztschr. f. klin. Med.,' iv, Hft. 1 and 2.

Yet the connection does not acquire its essential importance and really practical interest till we come to the consideration of chronic nephritis, which was selected by us as the starting-point of our discussion; our explanation must hold good here, if it is to have any value whatever. And it does hold good, unless I am utterly mistaken. For it makes it intelligible that the increase of arterial tension precedes the cardiac hypertrophy, and applies equally to the chronically inflamed large, and the small contracted, kidney, since the inflammatory disturbance of the circulation through the glomeruli and capillary meshwork gives rise to considerable resistance, which, it is true, is further augmented, or is exceeded, when many of the glomeruli are compressed and atrophied and numbers of the renal capillaries lost. Lastly, this obstruction of the flow through the inflamed kidneys is far from being done away with by the hypertrophy of the heart, which merely, as you will shortly hear, more or less compensates its effects on the secretion of urine. I may now venture to hope that you have ceased to perceive anything incomprehensible or enigmatical in the entire process. When the inflammatory changes in the kidneys have reached a certain degree of intensity and distribution, the arterial pressure begins gradually to increase, and this is necessarily attended by a similarly increasing hypertrophy of the heart. The *left* heart will, it is evident, be first affected, the hypertrophy being associated or not with dilatation of the cardiac cavity, *i. e. excentric or simple,* precisely as in the cases of stenosis of the aortic orifice or of general arterio-sclerosis. By far the most frequent change in these cases is in fact an hypertrophy of the left ventricle, which is sometimes enormous, and beside which the right chamber looks like a small appendage. Still, in many instances the hypertrophy of the left is followed by a similar enlargement of the right, heart—a circumstance which cannot surprise you after our discussion of the cardiac lesions. For the right side hypertrophy simply signifies that the increased bulk of the left ventricle has not sufficed to *completely* overcome the abnormal resistance of the very tense aortic system. All this, it is true, applies only to the pure, uncomplicated nephritis of comparatively young and strong subjects whose nutrition is fairly good; but to them it applies absolutely and without further qualification. I desire to emphasise this, in opposition to the statements of the ordinary text-books and to the opinion prevalent amongst physicians, who, while they acknowledge the great frequency of cardiac hypertrophy in contracted kidney, look upon it as comparatively rare in so-called chronic parenchymatous nephritis, *i. e.* in the large chronically inflamed kidney. So general is this the opinion, that it has recently been thought necessary in Frerichs' clinic* to describe in detail the clinical histories of several instances of large white kidney associated with hypertrophy of the heart, as though the object were to draw attention for the first time to this form of nephritis! In opposition to the very discrepant statements of different writers† as to the frequency of cardiac hypertrophy in association with the chronically inflamed large kidneys, I can assure you that during the many years in which I have attended particularly to this relationship, I have never met with a case of pure chronic nephritis in *fairly robust* individuals in which the hypertrophy of the heart was absent. Where at first sight it seemed to be so, more accurate examination always revealed the presence of *amyloid degeneration;* and although I readily admit the occurrence of geographical differences in certain forms of disease, I cannot avoid the suspicion that in English and German statistics of nephritis, the necessary discrimination between pure chronic nephritis and amyloid disease has not been rigorously carried out. The necessity of this distinction in the question now engaging our attention is sufficiently obvious; wherever amyloid substance makes its appearance we have to deal with individuals who are the subjects of some chronic cachexia or other—tubercle, syphilis, caries, &c., and in whom, consequently, there is an absence of one of the conditions indispensable to the production of a high arterial tension and the development of the cardiac hypertrophy.

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* Friedreich, in Canstatt's 'Jahresb.' f. 1857, iii, p. 194.

† Cf. Bamberger, l. c., p. 35.

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* Litten, 'Neue Charité-Annalen,' iv, S.-A., p. 1.

† Cf. Senator, 'Virch. A.,' lxxiii, p. 319.

The great length at which we have discussed the relation between renal inflammation and cardiac hypertrophy may perhaps be excused by you, on calling to mind the powerful influence which the hypertrophy must, and does in fact, exert on the functional derangement of the inflamed kidneys. The increase of arterial tension is accompanied, as you know, by an increase in the volume of the urine, while the quantity of solid urinary constituents is not augmented in the same proportion, and the urine therefore becomes lighter and paler. This is the effect which is exerted by the hypertrophy of the heart on the inflamed kidneys—certainly on the inflamed glomeruli, and still more energetically on those which have not become involved in the inflammatory process. In this way, the diminution in volume of the urine is approximately compensated in the large red or white kidney, *i. e.* in the subacute or moderately chronic form; while in markedly chronic nephritis, under the influence of which the most extreme degrees of cardiac hypertrophy are developed, the action of the hypertrophy in causing an increased secretion of urine may considerably exceed the effects of the inflammation and destruction of many glomeruli in diminishing it. That the urine loses its deep brownish-red colour and its high specific gravity when its amount is increased need not be mentioned expressly. When the quantity of urine is approximately normal, its specific gravity usually remains within normal limits, but where its volume is considerably increased the specific gravity becomes remarkably low, although the total quantity of urea and other solid constituents excreted in twenty-four hours need not at all be diminished. You see, then, that the disturbances of the normal renal function brought about by the inflammation are directly compensated by the cardiac hypertrophy and rise of arterial pressure. On the other hand, however, it cannot be expected that the escape of abnormal dissolved or formed constituents into the urine should be prevented or checked by the hypertrophy of the heart. When describing the urine secreted by these kidneys (vol. iii, p. 1180), I have, in fact, stated that in the chronically inflamed large kidneys it is cloudy and abounds in albumen, throwing down a copious sediment of blood-corpuscles, inflammatory corpuscles, and all varieties of casts; and though the secretion in the markedly chronic form which terminates in granular atrophy contains very little albumen and extremely few blood-corpuscles and casts, your attention has been drawn to the fact that this is thoroughly explained by the extremely insidious course and trifling amount of renal tissue involved at any one time in the inflammatory process. For that the cause of the albuminuria should be sought in these inflammatory changes and not in the cardiac hypertrophy and high arterial pressure may be inferred directly from our previous discussions, and I have, moreover, dwelt on this fact on a former occasion (vol. iii, p. 1151) to an almost superfluous extent.

During the course of chronic nephritis, we have not rarely an opportunity of convincing ourselves in one and the same patient of how greatly the constitution of the urine is influenced by the high arterial tension. For, as in the cardiac lesions, so here too *the compensation becomes inadequate*, either transitorily, *e.g.* under the influence of depressing emotions or intercurrent acute pyrexial affections, or definitively, when a complication, such as a valvular lesion or pericarditis, makes increased demands on the heart, and above all whe *the energy of the hypertrophied heart-muscle becomes exhausted*, whereupon, as you know, it usually undergoes fatty degeneration. So soon as, under these circumstances, the arterial pressure falls, the amount of urine at once decreases; not only in the large chronic hæmorrhagic kidneys, but also in the granular form, there may be a considerable diminution —to values of from 400 to 500 c.c., such as are otherwise reached only in acute Bright's disease. The more scanty the urine, the deeper will be its colour and the greater its concentration; yet, owing to the impairment of general health which accompanies the disturbance of compensation, the production of urea remains within moderate limits, and the specific gravity of the urine consequently seldom exceeds 1012—1015. Obviously, the percentage contents of albumen in the urine are also increased at this period. But that which in these cases is only a transitory or final phenomenon, is the rule in cases of chronic nephritis in which for any cause the rise of arterial pressure and cardiac hypertrophy have failed to set in. Hence, in senile contracted kidney there is usually no abnormal increase in the volume of the urine, and when a person with phthisis or disease of the spinal cord develops a pure chronic nephritis, you must not, for similar reasons, expect an abundant secretion of urine. Nor is the case essentially different with that alteration which without doubt is by far the most frequent and hence most important obstacle to the development of cardiac hypertrophy, namely —*amyloid degeneration* of the kidneys.

You know from former communications that the kidneys form one of the commonest seats of the amyloid process, and I need only supplement this by stating that we find almost no cases of somewhat advanced amyloid disease in which the kidneys are quite free from the change. Ever since this fact became more accurately appreciated, and in particular since we learned that amyloid degeneration plays an important *rôle* in very many cases which formerly were regarded as pure forms of Bright's disease, the clinicians, and pre-eminently Traube, have persistently endeavoured to acquire a knowledge of the influence which this change exerts upon the function of the kidneys, and by consequence on the constitution of the urine. Nevertheless, we cannot, unfortunately, so far claim to be in possession of adequate information with regard to the questions at issue. This is mainly owing to the *extreme inconstancy of the anatomical appearances in amyloid kidneys.* Even the amyloid change itself exhibits the greatest variations in its distribution. No doubt, we most frequently meet with degeneration of the glomeruli, next of the vasa recta, and least often of the capillary network; but between these we have all possible combinations. Sometimes the whole of the glomeruli are degenerated in the extreme; sometimes many are affected in their entirety, others in only a few of their loops; again it often happens that between the amyloid glomeruli a few are present which do not yield the least trace of the characteristic reaction. Further, the vasa recta are occasionally alone involved, at other times the vasa recta and the glomeruli; if the network of capillaries has undergone the amyloid change, the glomeruli are usually similarly degenerated, though it may also happen that only the vasa recta and capillaries are attacked. The small arteries of the cortex very commonly share in these various combinations, while the membrana propria of the tubules is but rarely involved, and probably only when the amyloid disease is extreme and widely distributed. More striking still than these irregularities, is the condition of the renal tissue proper in amyloid degeneration. In the first place, it is not so very uncommon to meet with kidneys which, except for the amyloid of the vessels, *do not present the least alteration of the epithelium or interstitial tissues.* In a second group of waxy kidneys *the epithelium of the urinary tubules* has undergone a more or less extensive *fatty degeneration,* when the interstices surrounding the markedly degenerated tubules are also full of fat-drops. But decidedly the most frequent change in the amyloid kidneys is a condition of *chronic inflammation;* we meet with both *large white,* and also, though more rarely, with *contracted, amyloid kidneys.* If we inquire into the signification of all these differences, it cannot reasonably be doubted that cases, in which the amyloid change involves only some of the glomeruli and that partially, or in which only certain portions of some of the vasa recta are diseased, must be regarded as comparatively *recent,* while an extensive degeneration speaks, on the contrary, for a relatively long duration of the affection. But as regards the much more interesting question of how it happens that the process begins on one occasion in the glomeruli, on another in the vasa recta, &c., we are absolutely without information. Moreover, with reference to the condition of the renal tissue in the waxy kidney, the chief importance has been attached by many to the alteration of the vessels, which is supposed to constitute the chief of all the changes: where the renal tissue is intact, we have, it is said, to deal with comparatively fresh cases; had the amyloid degeneration of the vessels lasted longer, there would have occurred fatty degeneration in the epithelial and interstitial tissues, leading to the destruction and loss of many epithelial cells, and thereby to cellular infiltration and thickening of the interstices. It agrees with this view, which is also defended by Weigert,* that where the amyloid change is extensive marked alterations of the tissues can hardly fail to be detected. Still I have not been so far able to convince myself of its exclusive applicability. In view of the facts acquired with reference to other organs, *e.g.* the liver, I raise no objection to the notion that the fatty degeneration of the epithelium should be regarded as the direct consequence of the disease of the vessels. Yet, in my opinion, the facts connected with the liver, &c., do not warrant our asserting such a relation of dependence for the true inflammatory alterations; for even in the most extreme and chronic amyloid disease we do not as a rule find the least sign of any inflammation in the liver, heart, lymphatic glands or intestine. Still less can it be supposed that the amyloid develops in the train of, and owing to, the chronic renal disease; this idea is negatived by the cases of amyloid of the vessels with the renal tissue intact, and, moreover, there is rarely any difficulty in determining the causes of the amyloid change. Accordingly, there is no alternative, it is clear, but to regard the nephritis and the amyloid degeneration as *two independent co-ordinated derangements*, which have attacked the same organ and probably in most cases are due to the same cause. This, in my opinion, is the simplest explanation of the occurrence of amyloid alone, or associated at one time with fatty degeneration of the epithelium, at another with true nephritis. For since syphilis, phthisis, chronic suppuration, &c., may bring about nephritis as well as amyloid degeneration, we must be prepared to meet one or other, or both together, when the kidneys become implicated, in such patients. In the latter case, it is evidently not necessary that both diseases should develop simultaneously; this is possible, but it is equally possible for the amyloid degeneration to precede the inflammation, nor is the development of the amyloid change in an inflamed kidney excluded. Moreover, if the amyloid degeneration and the nephritis are the effects of absolutely different causes—if, *e. g.* a gouty person with contracted kidneys acquires syphilitic amyloid disease—the two conditions will not follow any rule as regards their combination.

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* Weigert, 'Volkmann'sche Vortr.,' Nos. 162, 163.

Since such diversity prevails in the anatomical changes occurring in amyloid kidneys, it would clearly be absurd to expect the constitution of the urine to be identical in all these cases. With a view to becoming acquainted with the influence which the amyloid degeneration exerts on the renal function, it will be most advantageous to confine ourselves in the first instance to those kidneys in which the disease of the vessels either constitutes the only change, or is at most complicated by moderate fatty degeneration of the epithelium. Yet even in these simple cases a conclusion is rendered difficult by the fact that we have to deal in the great majority of instances with individuals whose constitution and general state have been undermined by more or less serious illness. What the primary disease fails to accomplish in this direction is effected by the amyloid degeneration, regularly distributed as it is over the different organs. The great majority of the individuals with waxy kidneys are anæmic; very many of them have hectic fever, others have œdema, and not a few suffer from severe digestive disturbance, if for no other reason, because of the intestinal amyloid. All these matters are obviously of importance for the urinary secretion, but they act partly in very different directions. While the anæmia causes *per se* an increased secretion of urine, pyrexia, œdema, and above all profuse diarrhœa are factors which tend to diminish its amount; again, the production and excretion of urea suffer in consequence of the diarrhœa, but are furthered by the pyrexial rise of temperature. It cannot, therefore, excite surprise that the *picture presented by the urine in pure amyloid kidneys* is an extremely variable one as regards amount, colour, urea-contents, and specific gravity; and though it may be stated in general that the patients in question, when not labouring either under diarrhœa or pyrexia, pass a fairly large quantity of pale yellow urine, with somewhat diminished urea-contents, and a specific gravity keeping close to the normal values, there are many exceptions to this rule. Thus, in many cases the strikingly large amount of the urine, which is always of low specific gravity, attracts attention; this is sometimes observed to persist for a time, or it may give place on alternate days to a diminution of the secretion. The most unquestionably constant character of the pure amyloid urine is its *clearness;* it contains extremely few blood-corpuscles and casts, if any, and scarcely throws down a sediment on standing. This character is the more noteworthy, since considerable quantities of *dissolved albumen* are present, as a rule. A contents of 1—2 per cent. albumen is quite common in pure amyloid urine; occasionally even larger quantities are observed, and certainly this variety of urine is one of those most rich in albumen. Yet you will clearly understand—*as a rule only.* For we meet with amyloid kidneys that secrete urine which is at least temporarily, and may be lastingly, free from any trace of albumen, and Bartels is in error when he categorically denies that albuminuria may be absent in amyloid disease of the kidneys.* I have myself several times seen amyloid kidneys in people whose urine, according to the statement of their medical attendant, never yielded the reaction of albumen; by clinicians also this has repeatedly been observed,† and Weigert‡ rightly remarks that in cases of amyloid associated with marked albuminuria it is impossible to say whether the amyloid degeneration has from the start been attended by albumen in the urine. However great the probability, therefore, of an amyloid degeneration of the renal vessels when the urine is clear, pale yellow, approximately normal in volume and specific gravity, and containing a large amount of albumen, especially when tuberculosis, syphilis, or any of the diseases known to give rise to the amyloid change is present, yet the non-occurrence of the degeneration of the vessels cannot be certainly inferred from the absence of albumen. Still it would be easy to submit to this diagnostic inconvenience, if only some light were shed by it on the nature of amyloid albuminuria. On this point the most different assumptions have been entertained. By many writers it is absolutely denied that mere amyloid of the vessels gives rise to albuminuria, which only sets in after the disease of the vessels has become complicated by fatty degeneration of the epithelium, or by nephritis—a view shown to be false by Traube, who pointed out the existence of kidneys in which the vascular amyloid was the only disease of the tissues present. The attempt to explain the albuminuria in pure amyloid kidney by the fall of blood-pressure due to the constitutional disease, is rendered abortive by the fact that the quantity of albumen excreted far exceeds that escaping into the urine as the result of a lowered blood-pressure; still less tenable is the opposite view, according to which the albuminuria is caused by a rise of blood-pressure in the non-affected glomeruli, which itself depends on the imperviousness of the degenerated ones. This abnormal resistance on the part of the amyloid glomeruli is rather a subject for theoretical discussion than an actually demonstrated fact. We are completely ignorant as to the state of the circulation in amyloid vessels, and if on artificially injecting the kidneys post mortem, some of the glomeruli or a few of their loops do not take the injection, this, it is easy to understand, does not prove anything as regards the circulation during life. Accordingly, all attempts to explain the origin or the absence of albuminuria from the mode in which the blood circulates through the degenerated glomeruli are, in my opinion, purely illusory. So far as I am concerned, the hypothesis started when this disease was first recognised still appears the most plausible one—that *the vessels become abnormally permeable to dissolved albumen in consequence of the amyloid degeneration.* It is naturally the glomeruli that are here chiefly con-ned, and it is therefore not without interest that in many cases of non-albuminous urine, the amyloid change has been found to involve exclusively, or at least very preponderatingly, the vasa recta. Nevertheless, it would be an error to look upon this as a law; even in waxy degeneration of the glomeruli, the absence of all albuminuria has been repeatedly determined. As to the cause which, despite the abnormal permeability of the glomeruli, prevents the escape of albumen into the urine, I am unwilling to speculate, more especially as we do not possess any thorough investigations into the condition of the glomerular epithelium in amyloid disease of these vessels. While our inability to discover in the condition of the diseased vessels themselves or in that of the remaining renal tissues any reason for the non-occurrence of albuminuria is, it is true, a lamentable defect; yet this fact does not seem to me to constitute any insuperable objection to the hypothesis of an increased permeability of the amyloid capillaries to dissolved albumen, an hypothesis which is better adapted than any other to render intelligible the peculiar constitution of the amyloid urine,—*the abundance of albumen and the almost complete absence of formed elements.*

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* Bartels, l. c., p. 463.

† Cf. Litten, 'Berl. klin. Wochenschr.,' 1878, No. 22; 'N. Charité-Annalen,' iv, S.-A., p. 21; Rosenstein, 'Path. u. Ther. d. Nierenkrankheiten,' p. 258; Wagner, 'M. Br.,' p. 327.

‡ Weigert, loc. cit., p. 17.

It is very different with the urine in *amyloid nephritis*, *i. e.* in those cases which are characterised by the combination of amyloid degeneration of the vessels with typical inflammatory alterations. This form embraces, as already mentioned, first the "large white kidneys" of English writers, which in their descriptions they have unfortunately included with the pure non-amyloid, chronic nephritis. Bartels, who willingly adopted the view of English pathologists, even states expressly that in chronically inflamed kidneys the small arteries and Malpighian tufts are very frequently found in a condition of amyloid degeneration,* but, strange to say, he fails to see herein a reason for distinguishing this frequent form from that in which the amyloid is absent. In this way is to be explained the occurrence, in Bartels' description of his chronic parenchymatous inflammation, of many statements which, if maintained with regard to the large amyloid nephritic kidneys, I should be unwilling to subscribe to; more especially the asserted retrogression of the process, so repeatedly emphasised by him; for that a large white amyloid kidney can ever become "retrograde" appears extremely doubtful. On the other hand, you may safely infer from this procedure of Bartels that the functional disturbances occasioned by simple and by amyloid chronic nephritis have a strong resemblance, or indeed are identical, in many respects. In fact, the urine in large, white, amyloid kidneys, or—to use a favourite term in this country—the *waxy* or *butter-kidney*, is always *rich in albumen* and *in formed constituents*; it has a deep red colour, is rather cloudy from the first, and throws down a sediment in which red corpuscles are present only in small numbers, but which contains colourless corpuscles, besides casts of every kind, together with fattily degenerated epithelium and masses of fatty detritus. True, the urine is not usually quite so cloudy as in simple chronic nephritis, nor is the sediment so rich in colourless blood-corpuscles and casts, without doubt because the amyloid glomeruli permanently retain a certain degree of impermeability towards formed constituents. On the other hand, the amount of dissolved albumen present is wont to be still greater than in non-amyloid chronic nephritis; 3, 4, or even 5 per cent. albumen has repeatedly been found in such cases, and Bartels is right in drawing attention to the fact that such large quantities of albumen are not discharged in any other form of renal disease. But the increased percentage excretion of albumen is greatly due to a circumstance by which the urine of chronic amyloid nephritis is wont to be essentially distinguished from pure chronic Bright's disease—I mean *its small volume*. This diminution in the amount of urine secreted is not, it is true, always equally great; yet it is mostly really considerable; for weeks and months together the daily volume may be approximately from 400 to 500 c.c. The urine has then a dark red colour, and, owing to its reduced amount, a high specific gravity, although the absolute quantity of urea excreted daily remains, as a rule, considerably below the normal. I need hardly say to what this important difference, as compared with the urine of Bright's large kidneys, is due; for you know that it is through the hypertrophy of the heart that the latter acquires its larger volume and clearer colour, and in the characters of the urine of amyloid nephritis, as just described, you recognise the direct result of *the absence in these cases of increase of arterial tension and cardiac hypertrophy*. The excessive richness of the urine in albumen in these diseases is obviously due to the abnormal permeability of the amyloid glomeruli towards the dissolved albuminous bodies of the blood-serum.

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* Bartels, l. c., p. 312.

The other variety of chronic amyloid nephritis, the *amyloid contracted kidney*, is much rarer than the large white amyloid kidney. Its comparative rarity is simply explained by the fact that the time requisite for the production of granular atrophy is not allowed in the case of persons so seriously diseased. On the other hand, however, the long duration and extremely protracted course of nephritis terminating in contraction admit of a result which could hardly occur in less chronic forms, namely *the establishment of amyloid degeneration in kidneys already granular*. In this case the cardiac hypertrophy is not absent, and the urine of such kidneys is distinguished from that of the pure contracted form solely *by its large albuminous contents*. But if the amyloid degeneration be not merely a late complication of renal contraction, and have arisen *pari passu* with the chronic nephritis, an hypertrophy of the heart will fail, for the well-known reasons, to occur, and the urine will acquire characters which have often led the physician astray. Owing to the absence of all extensive, active inflammation, it is *clear*, *pale*, contains *very few formed constituents*, and hardly throws down a sediment. But, in consequence of the amyloid disease of the vessels, it is *rich in albumen*, and would therefore closely resemble the pure amyloid urine, were it not that, as a rule, its volume is abnormally *reduced*. True, this diminution is far from being so considerable as in the large white amyloid kidney, yet not more than a litre to 1200 c.c. is passed. With this scantiness, again, the comparatively low specific gravity—on the average 1010 to 1012—is wont to contrast, so that this urine unites in itself some of the characters of the secretion in the most different forms of nephritis.*

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* Cf. Wagner, 'Morb. Br.,' p. 329, *et seq.*, who believes, according to his experience, that the sharp distinction of the urine of the pure amyloid from that of the amyloid nephritic kidney is somewhat arbitrary, and hardly to be carried out in practice.

All that I have hitherto told you of the inflammatory functional disturbances of the kidneys refers exclusively to the *non-suppurative forms* of nephritis. Now there occur, as I indicated at the outset, purulent renal inflammations, which, obviously infective in character, run a very different course and have a different anatomical localisation and distribution. Passing over direct infected wounds, it is chiefly the circulation that conveys the excitor of inflammation to the kidneys, and conformably to our more accurate knowledge of the nature of the various pyogenic poisons, we are able in many of these cases of suppurative nephritis to accurately demonstrate the cause of inflammation in the form of characteristic *colonies of bacteria*. I have principally in mind the small foci which are so often found in the bodies of persons who have perished from *pyæmic*, *septic*, or other allied process, but which are especially characteristic of *endocarditis ulcerosa*. In this latter disease they are usually met with in really astonishing quantities, distributed over the whole kidney, cortex as well as medulla—the medulla being the favourite situation of the foci in the septic processes—and one is struck at the first glance by the presence, both on the surface of the organ and of the section, of *innumerable grey or greyish-yellow specks and streaks*, which are often, but not always, marked off against the remaining renal tissues by small rings of hæmorrhage. Microscopic examination shows them all to be necrotic, necrotic purulent, or purulent hæmorrhagic foci, the centres of which are invariably occupied by smaller or larger *groups of micrococci*. It is usually possible to make out the situation of the groups, which occupy the interior of blood-vessels; and this can easily be shown to be the location of the many colonies which microscopic examination proves to lie outside the small foci in the midst of the perfectly normal and absolutely unaltered tissues of the vicinity. The larger groups of micrococci are situated in the smaller arteries of the cortex or medulla, and are sometimes delicately branched as they follow the ramifications of the vessels; some of the small colonies occupy the glomeruli, but most of them are found in the meshwork of capillaries. The foci caused
are, as already stated, minute, and rarely exceed one
re in diameter; yet even when they attain this size

some of the urinary tubules in the neighbourhood will be found to be included.

But the fact that when necrotic inflammatory or completely purulent foci are discovered in the kidney, their centres are occupied by unmistakable groups of micrococci does not allow of our concluding without further evidence that the latter have been carried into the positions occupied by them from the a. renalis. For there is a second path by which the exciter of inflammation may reach the kidneys, a path which I pointed out at the commencement of our discussions on nephritis—I mean the *ureter and pelvis of the kidney*. Non-suppurative nephritis never, so far as we yet know, originates in this way; but this mode of infection is all the more important as regards the suppurative form. It is thus that *pyelonephritis* arises, a very important and justly dreaded affection, which is deserving of attention, if for no other reason, because it was the first in which colonies of micrococci were demonstrated—by Klebs, as is well known—in the human organism. In this disease, as you doubtless remember (cf. vol. i, p. 345), the schizomycetes, after having passed from the bladder through the ureter into the pelvis of the kidney, enter the open collecting tubules of the papillæ, and penetrate, against the stream of urine, through the straight tubules high up into the cortex; and wherever they remain fixed and multiply to form large masses they give rise to a necrotic purulent inflammation in their immediate neighbourhood. Accordingly, the pyelonephritic purulent foci always have a linear form, which corresponds precisely in direction to the straight urinary tubules. The pyelonephritis is sometimes unilateral, but both kidneys are much more frequently affected; the number of foci varies extremely, from a few to such multitudes that the surface of the section becomes striped with yellow lines, extending from the pelvis in the direction of the superficies, while the surface of the organ is thickly dotted over with yellow spots. The size of the individual foci is equally varied; they may consist only of short streaks, or may extend from the papilla to the surface of the kidney, and between these two extremes there may be every conceivable gradation. The transverse diameter of the foci is usually slight, but the confluence of neighbouring ones may give rise to broad zones of suppuration. The seat of this purulent inflammation is obviously the vascular interstitial tissue; yet it is no less obvious that the tubules included in the foci will also be involved. The epithelium of the tubule containing the colony is of course already necrotic before the purulent inflammation begins; but that of the remaining tubules, bathed in purulent exudation, cannot possibly preserve its integrity.

While it is characteristic of these suppurative renal inflammations that they appear *in the form of foci*, this applies with still greater force to the larger collections of pus in the kidneys, the true *abscesses*. These, as already stated, are either of *traumatic* origin, or they are constituent phenomena of that severe *pyæmic* process, in which abscesses develop in all possible organs, in the kidneys, liver, lungs, brain, spleen, muscles, joints, &c. The kidneys, it is true, are far from being so frequently involved as the liver and lungs, yet they are by no means low down in the scale of frequency. These abscesses also vary greatly in dimensions, from mere "miliary" foci to the size of a potato, or more; but whether small or large they consist solely of true, greenish-yellow pus, which as a rule has a viscid consistence; within their area all the renal tissues have perished. Yet however voluminous these abscesses, well-preserved renal tissue always remains in the vicinity; for *a diffuse suppurative inflammation involving the whole kidney never occurs.*

From this fact it directly follows that even the most severe suppurative nephritis cannot give rise to complete anuria. Should you, however, inquire, what then are the functional disturbances occasioned by purulent inflammation of the kidneys, I cannot give you much positive information. These cases are not usually simple and uncomplicated, for we have in the great majority of instances to deal with severe pyrexial disease, in which many things contribute to disturb the secretion of urine; and in pyelonephritis we meet with the additional difficulty that the urine passed by the patient and handed to us for examination is not the unaltered renal secretion, but contains mixed with it the products of the puru'ent pyelitis, and frequently too of a ureteritis and cystitis.
ıe formed constituents of the urine must certainly be re-

ferred to these complications, and mainly to the pyelitis; they are present in such quantities that the urine is quite cloudy when passed, and deposits a copious sediment. The sediment, however, is essentially distinguished from that of non-suppurative nephritis; for by far the greater part of it consists of *pus-corpuscles*, compared with which the red blood-corpuscles are, as a rule, in a great minority; in addition it contains epithelial cells whose shape allows no doubt that they are derived from the pelvis or bladder, and not from the kidney itself; *no casts are present in the sediment*, but the freshly passed urine very often swarms with bacteria. It is further characteristic of the urine of pyelonephritis that it contains only *minute quantities of dissolved albumen*; its reaction is frequently alkaline, which is decidedly exceptional in nephritic urine. On the whole, the urine gives one the impression of being the *normal, but no longer fresh, secretion, with which a quantity of pus had been mixed*. Even in cases of suppurative nephritis where the large urinary passages are intact, we are not justified in at once attributing every abnormality of the urine to the renal affection. If, *e. g.* the urine contains a little albumen, and is somewhat reduced in amount, both these changes may very well depend on the pyrexial septic general affection, which equally attends the small multiple, as well as the large, renal abscesses. These in fact constitute in most cases the only changes presented by the urine, so that a diagnosis of this form of purulent nephritis based upon the characters of the urine is altogether out of the question; for even should the urine contain a few pus-corpuscles, this does not allow of our distinguishing it from simple pyrexial albuminuria. Under these circumstances, the urine in purulent nephritis has perhaps a greater negative than positive pathological interest. For if in such a severe interstitial inflammation, by which innumerable urinary tubules are affected, owing to the number of the foci when these are miliary, the urine does not contain a quantity of albumen worth mentioning, nor any formed constituents, in particular casts, this fact apparently constitutes a noteworthy indication of *the high degree in which the glomeruli contribute to the production of the albuminuria and urinary sediment in renal inflammation*. This conclusion would, it is true, be more acceptable, were we able to define the share which the tubules included in the foci take in the secretion of urine. Why the glomeruli from which these tubules spring should not go on secreting—provided they are not themselves included in the foci—appears impossible to explain; yet we are ignorant as to whether the tubular lumina within the foci are not obliterated by the pressure of the surrounding exudation or blocked by dead epithelium. Were this the case, it would not be specially remarkable that the purulent foci do not betray their presence by any change in the urine; and in any case this point must be decided before suppurative nephritis can be successfully utilised for the theory of albuminuria and cast-formation.

What we have determined with regard to suppurative nephritis applies also to *tuberculosis*. It has no influence on the constitution of the urine, because, as may certainly be assumed here, the urinary tubules included in the tubercular foci no longer participate in the secretion of urine; only when tubercular pyelitis is simultaneously present can the urine contain the characteristic *bacilli*, in addition to the products of tuberculous disintegration and caseous detritus. It need hardly be mentioned that solid *tumours* of any kind are incapable of altering the characters of the urine; for they produce no disturbance of the renal function except that arising from the loss of secreting substance. The same thing applies to the *infarcts* of the kidney, at least if we disregard the slight *hæmaturia*, which often accompanies their formation.

Having hitherto minutely discussed the *inflammatory* alterations of the membranes engaged in the secretion of urine, it only remains to consider the changes that may take place in these membranes through other causes, and the influence of these changes on the urinary secretion. And here we have to deal first with a disease, to which reference has repeatedly been made in this section, namely *cholera*. I have referred to the anuria occurring during the attack, and to the striking poverty in salts of the urine passed after it—both the readily intelligible results of the enormous loss of water and salts in [illegible] dejections. I told you, further, that the urine occasionally contains albumen during the paroxysm and previous to the occurrence of anuria, owing to the fall of blood-pressure and retardation of the flow, and that after the attack albumen is never absent from the urine; to this latter, the typical *cholera-urine,* I should now like to devote a few words That the urine which is passed after the attack is very markedly distinguished from the normal secretion, naturally attracted attention during the first cholera epidemic, and then too it was demonstrated that albumen is one of its constant constituents. Later on, when the formed constituents—blood-corpuscles, epithelial cells, and more especially casts—were discovered, there was no hesitation in regarding these as the signs of a renal inflammation; and thus we find Frerichs, for example, looking upon cholera as one of the causes of morbus Brightii, or citing the renal affection following cholera as one form of Bright's disease. This view is quite conceivable *per se,* and this form of nephritis must then be explained in the same manner as are those following scarlet fever and other infective diseases. Nor would it make against this interpretation that no interstitial thickening or infiltration is found in the kidneys of persons dying in the stage of reaction, when the urinary change is at its height; for these are also absent in that acute form of inflammation which we have termed glomerulo-nephritis. Yet the course of the renal affection in cholera is altogether different from that in other acute diseases, and is above all much shorter than has ever been observed in actual nephritis. In the convalescent, the diminution of the urine lasts only a few days, and often as early as the third day gives place to a steadily increasing augmentation, which may ultimately amount to an actual, though brief, polyuria; after from six to eight days this also has usually passed off, and the volume of the urine returned to the normal. Much earlier than this, when the secretion begins to increase, the abnormal constituents—casts, epithelial cells and blood-corpuscles—disappear from the urine; the dissolved albumen is somewhat slower in disappearing, but the secretion, once it has become abundant, is usually free from it. On the other hand, should the stage of reaction take an unfavorable turn, in particular if so-called *cholera-typhoid* develops, the albumen persists and the urine continues scanty till death; though in the last days of life casts are usually absent from the sediment, which consists chiefly of urates, and, in addition, of pus-corpuscles and epithelium from the bladder, if, as so often happens, a catarrh of the bladder has been set up by frequent catheterisation. But, as Bartels very rightly states, cholera never gives rise to a true acute or chronic nephritis.*

But we can afford to dispense with the assumption of a renal inflammation, since a perfectly adequate cause of the renal functional disturbance is presented by the severe *derangement of the circulation*. The great inspissation of the blood leads to anuria during the attack; and because this inspissation only gradually passes off, and the watery contents of the blood and the arterial pressure are only gradually restored to the normal standard, the diminution of the urine persists for the first few days after the paroxysm. Remember, further, how very sensitive the epithelium of the glomeruli is to every disturbance of the regular circulation through the tufts; for if compression of the renal arteries for a brief period suffices to render the urine albuminous, can it excite surprise that the same effect should follow, when, for a great number of hours together, the glomeruli are only supplied by an extremely feeble stream of profoundly altered blood? Moreover, the amount of albumen excreted in the urine during the stage of reaction is always small, and it is only the trifling quantity of urine passed during the first few days that makes an impression to the contrary: immediately on the volume of the urine increasing, it contains—in marked contrast to true nephritis—at most a few parts of albumen per thousand. Simultaneously with the excretion of albumen, there will always, of course, be an escape of colourless, and a few red, corpuscles into the urine. All this ceases, however, when, owing to the restoration of a normal circulation, the glomerular epithelium loses its abnormal permeability and recovers.

Yet this, you are aware, is not the only effect exerted by the choleraic process on the renal function. The kidneys of a person dying a few days subsequently to the seizure present a more or less striking contrast between the pale grey to yellowish-grey, opaque cortex and the bluish-red medulla. On microscopic examination, the whole of the epithelium of the cortex is found to be markedly granular, and in many places full of fat-drops, while numerous casts occupy the straight tubules. Moreover casts are never absent from the urine of the stage of reaction, being hyaline, fatty, and granular, of all degrees of thickness, and often of surprising length; accompanying these, epithelial cells are constantly met with, either single or forming larger adherent shreds, and derived from all parts of the urinary organs, from the tubules to the bladder. The presence of these formed constituents causes the urine passed at the commencement of the stage of reaction to be *cloudy, brownish red* in colour, and *mixed with flakes and shreds.* That evacuated later becomes clearer and clearer, because the coarse epithelial elements and afterwards the casts become gradually more scanty, till they—even in unfavorable cases—completely disappear. All this is evidence that the urinary tubules also are seriously affected by the choleraic seizure, and Litten* has recently succeeded in experimentally producing conditions similar to those that prevail in cholera. For he has shown, as I recently reported (vol. iii, 1166), that when in a rabbit the kidney is deprived for from one and a half to two hours of its arterial supply, a very considerable portion of the epithelium of the tubules succumbs to *coagulation-necrosis*, which is distinguished by a great tendency to subsequent *calcification.* Whether coagulation-necrosis occurs in cholera-kidney we do not know, simply because at the time of the last great epidemics—that of 1866, for example, in which my own knowledge of the disease was acquired—we were still unacquainted with this important form of necrosis; the determination of this point must therefore be reserved for the future. Calcification, at any rate, *never* occurs in the cholera-kidney. Yet this fact does not constitute any obstacle to our applying Litten's experiences to the kidneys in cholera. For in the choleraic seizure the renal circulation is never so completely interrupted as in Litten's experiments; however inspissated the blood, its flow through the kidneys may indeed be extremely retarded, but *it cannot cease altogether, so long as the heart*

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* Bartels, l. c., p. 207.

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* Litten, 'Ztschr. f. klin. Med.,' i, Hft. 1.

continues to beat. Hence, we should not be justified in certainly assuming that a true coagulation-necrosis of the urinary tubules occurs. It is possible that individual cells die, that only portions of the cell-substance of others perish, while other cells may perhaps undergo simple fatty degeneration—in short there is an abundance of possibilities; and if any one should prefer to attribute the formation of the casts to the epithelium, or again to the coagulation of the albumen transuding from the glomeruli, he may do so freely in cholera; the conditions necessary to either mode are amply afforded. Taking everything into account, you will now admit that there is no evidence whatever for the existence of a *cholera-nephritis*: inasmuch as all the other peculiarities of the urine*—the urea-contents, specific gravity, salts, &c.—may easily be explained by a reference to the condition of the blood, we shall not hesitate to regard, with Bartels, the choleraic renal affection as solely the direct result of the severe circulatory disturbance brought about by the attack of cholera.

While the conditions on which the alteration of the urinary secretion in cholera depends are sufficiently apparent, this is not the case in another disease, where the state of the urine compels us to assume an alteration of constitution in the filtering membranes. The change in the urine with which we are here concerned early attracted attention, inasmuch as no chemical examination was necessary to determine its nature, apparent as it is at a glance,—I refer to *chyluria*.† The characteristic feature of this affection is the resemblance of the urine to milk, or rather to the chyle which flows during digestion through the thoracic duct. This latter comparison is the more apt, since the urine owes its opaque appearance to the presence in it of immeasurably minute *fat-molecules*, identical with those which are contained in the chyle; and like the chyle, so too the chylous urine cannot be rendered clear even by passing it through a double filter-paper. To make the resemblance still more pronounced, the chylous urine always contains albumen, very often coagulable, so that large clots separate out from it, while in certain circumstances the entire urine may stiffen. We have always to deal simply with a mixture of fat and albumen with the urine; the quantity of each substance varies considerably not only in different persons but in the same individual; still the albumen does not easily exceed 1 per cent., while the fat as a rule falls short of this even in the most pronounced cases. As for other, morphotic, elements, casts are never present, but some blood-corpuscles are usually found, and may occasionally be so numerous as to give the chylous urine a reddish tinge; it is also quite common for the galacturia to be preceded by a period of hæmaturia. In all other respects the urine of these patients is normal; it presents no peculiarities as regards reaction, amount, specific gravity, or urea-contents; the absence of sugar is also expressly stated by different observers.

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* A very accurate account of the cholera-urine is given by Bruberger, 'Virch. A.,' xxxviii, p. 296. Cf. also Buhl, 'Zeitschr. f. rat. Med.,' N. F., vi, 1855, p. 1; Wyss, 'A. d. Heilkunde,' 1868, p. 232.

† Israel, 'Virch. A.,' lxxxvi, p. 299.

Chyluria, according to all accounts, is a very common disease in the tropics. In the great majority of the cases observed in Europe, the patients have been persons who had lived a considerable time in tropical countries, such as Brazil, and were either diseased before returning home, or developed the affection afterwards. Cases of galacturia in individuals who have never been out of Europe are extremely rare.[†] Once the disease is established, it runs its course with marked remissions and intermissions, and is in general very intractable. In some persons the urine has a more or less milky appearance for many years, though, on the other hand, complete recovery has also been observed. It may as well be noticed here that the general well-being is in no respect seriously disturbed by the chyluria.

As to the cause of this striking alteration of the urine, we are so far unacquainted with any anatomical change that would throw light on it. In the few reports of autopsies of persons who had suffered from chyluria, we are usually assured that the kidneys were perfectly intact. It is claimed in a

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[*] Cf. Ackermann, 'Deutsch. Klinik,' 1863, Nos. 23, 24; 'D. A. f. klin. Med.,' i, p. 128; Thiry-Mieg, 'Gaz. méd.,' 1868, No. 19; Eggel, 'D. A. f. klin. Med.,' vi, p. 421, also contains references to the literature.

[†] Oehme, 'D. A. f. klin. Med.,' xiv, p. 262; Brieger, 'Ztschr. f. physiol. Chemie,' iv, p. 407; 'Charité-Annalen,' vii, Jahrgang 1882.

few instances that an abnormal communication was present between a lymphatic vessel and one of the large urinary passages, as *e. g.* a lymph-fistula discharging into the bladder; but if so, there must have been present in addition either a very unusual arrangement of the lymphatics, or a permanent or temporary stagnation of chyle in the thoracic duct, in order that the chylous, and not simply lymphatic, character of the urine may be adequately explained. Still this might perhaps occur, and may be the explanation of the isolated cases of European galacturia. To assume this, however, of the so frequent hæmaturia and chyluria of the tropics would be altogether too hazardous. True, on considering in what other way the urine could acquire this chylous character, it appears that several circumstances must unite to produce it. Since, namely, the characteristic constituents of the chylous urine, *i. e.* the intimate mixture of albumen, partly coagulable, and minute molecules of fat, cannot well enter the urine unless first contained in the blood, we postulate, first, that the composition of the blood is at least so far altered that its serum contains those immeasurably fine fat-droplets, which are normally found in the chyle but not in the blood. With this postulate it is in conformity that an increase in the fatty contents of the urine has been observed in several cases during the period of digestion; not only so, but in the case described by Eggel* direct proof was afforded that the blood was actually thus altered: the blood obtained from this patient by cupping contained very large quantities of the minute fatty molecules. In Brieger's case,† on the contrary, both the microscopical and chemical examination of the blood for fat gave a negative result; nor did an increased supply of fat with the food augment the fatty contents of the urine, though when fat was withdrawn, the otherwise chylous urine, passed on waking, became clear and bright, and at the same time poorer in albumen. The abnormal constitution of the blood, however, would not alone be sufficient, you are aware, to render the urine albuminous and chylous; in persons whose kidneys were perfectly intact, the urine would still retain its normal characters. As to the cause of this abnormal constitution of the blood we know nothing; and I refrain in particular from deciding how much confidence should be reposed in the statements of Lewis,* who claims that, in the blood of persons suffering from chyluria, he has regularly found entozoa, which are called by him *filaria sanguinis hominis*. On the other hand, the alteration in the kidneys, which, so far as I see, must necessarily be presumed to exist, can scarcely be anything but an abnormal permeability of the glomeruli and especially of their epithelium. I do not fail to see that we here enter the region of pure hypothesis; nor can anyone who asks himself, for example, why this urine, rich as it is in coagulable albumen, never contains casts, remain insensible to the imperfections and inadequacy of our attempted explanation.

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* Eggel, 'D. A. f. klin. Med.,' vi, p. 421.

† Brieger, 'Ztschr. f. physiol. Chemie,' iv, p. 407; 'Charité-Annalen,' vii, Jahrgang 1882.

We have still to consider some conditions, of which it has long been known that, under their influence, the urine is altered in constitution and in particular contains albumen, without our being able so far to satisfactorily account for the fact. Many of these cases belong to the category of so-called *hæmatogenous albuminuria*, an albuminuria, that is, which depends upon an imperfection in the composition of the blood. The supporters of this category have, it is true, fallen off considerably in the course of time, and with good reason, in so far as it was chiefly thought that the albuminous bodies of the blood had undergone a change of constitution; for in true pathological albuminuria such a change can hardly ever come into question. Senator† has, however, recently drawn attention to the view that *quantitative* changes in the composition of the blood may be of importance in this respect. Influenced by our experience as to the filtration of solutions of albumen containing salts, he considers that even an unusual richness of the blood in *salts* may perhaps give rise to an escape of albumen into the urine, and is inclined to ascribe a like effect to an abnormally large urea-contents of the blood. The first factor, the richness in salts, may explain the so-called *albuminuria of digestion*, *i. e.* the appearance of albumen in the urine of many persons some time after an abundant meal; while the increased urea-contents of the blood may be of importance in the albuminuria of *fever*, acute *phosphorus-poisoning*, and similar processes. As regards fever, Senator also points out that the *increase of temperature* alone may perhaps render the albumen more easily filtered, and may thus constitute one of the causes of the commonly occurring albuminuria. That all these points *may* have more or less importance for the urinary excretion, I am far from wishing to dispute; on the contrary, I believe that a great service has been done in directing attention to them. Still, I should like to remind you that possibly the connection between these alterations in the physical or chemical constitution of the blood and the albuminuria may be much less direct than Senator supposes. We formerly (vol. iii, p. 1153) arrived at the conviction that every considerable disturbance of the circulation renders the membranes taking part in the secretion of urine permeable to albumen; may not the same result be produced by *considerable alterations in the constitution of the blood?* I have referred to this possibility on another occasion (vol. iii, p. 1125), and am the more unwilling to leave it out of account, as it receives unmistakable support from some new experiments of Grützner.*

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* Lewis, 'The Lancet,' 1873, i, Nos. 2, 19. Cf. also note on p. 495, vol. i.

† Senator, 'D. Albuminurie,' &c., p. 87, *et seq.*

In the foregoing exposition, the *epithelium of the urinary tubules* has frequently come up for discussion; its possible participation in the formation of casts has repeatedly been considered; and we have ventilated the question of the importance of alterations, in particular of loss, of the epithelium as regards the passage of albuminous bodies from the blood into the urine. But in all the cases previously discussed, there were present at the same time serious alterations in the vessels, mainly of inflammatory or amyloid nature, and it was the existence of this combination that rendered the estimation of the importance of the epithelial change so very difficult. Accordingly, if our object be to learn what influence pathological conditions of the epithelium of the urinary tubules exert on the secretion of urine, our attention must naturally be confined to kidneys, in which changes other than those of the epithelium are as far as possible absent. Yet the prospect of thus arriving at a conclusion is rather dubious. If we disregard necrosis and loss of epithelium, only two morbid conditions which often affect the epithelium of the convoluted tubes are recognised by pathological anatomy, namely, *cloudy swelling* and *fatty change*. Now the kidney, when in a condition of cloudy swelling, is usually free from inflammatory or other change; still the possessors of such kidneys invariably suffer, as you will remember from a former discussion (vol. ii, p. 685), from a pyrexial or at any rate severe constitutional disease, which *per se* cannot fail to react on the urinary secretion. If a rather scanty, mostly reddish-yellow urine, containing a small quantity of albumen, is secreted by kidneys which have undergone parenchymatous degeneration, you know that the urine acquires precisely these characters in fever and when the arterial blood-pressure is low; so that it is consequently impossible to say whether cloudy swelling as such has anything to do with this condition of the urine. Nor is the prospect much better as regards the *fatty change*. In many animals, *e. g.* dogs and cats, the epithelium of the straight tubules of the cortex is almost at all times full of fat-drops, whose origin is unknown; in man, on the contrary, such a, if you will, physiological fatty change never occurs; and when it arises pathologically, the straight tubules are involved only in very extreme cases, the tubuli contorti being the typical seat of the affection. We are well acquainted up to a certain point with the mode of origin of fatty changes in man (cf. vol. ii, p. 662, *et seq.*), for we found that the real determining factor is the deficient supply of oxygen to the cells involved, whether this depends on general causes, or is the result of an interference with the arterial blood-stream to the affected organ. Now the bare mention of these causes is enough at once to show you that the fatty change of the renal epithelium must always be complicated by some general affection or by a disturbance of the circulation in the kidneys themselves. This applies equally to the fatty kidneys of the aged and the phthisical, the anæmic and the icteric, as well as to the fatty changes depending on inflammation, amyloid disease, sclerosis of the renal arteries and venous hyperæmia, to the phosphorus- as well as to the cholera-kidney. In fact, there exists, in all these cases, sufficient reason for an altered constitution of the urine to render it unjustifiable that we should make the fatty change of the epithelium responsible for it. Not only so, but the not exactly infrequent observations, according to which, for a time at least, the urine is perfectly free from albumen in acute phosphorus-poisoning, pernicious anæmia, and the fatty kidney of old age, render the dependence of the albuminuria on the fatty change of the epithelium rather improbable. Analogous considerations forbid us to conclude from experiences at the sick-bed as to the influence of the fatty change on the excretion of urea.*

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* Grützner, 'Pflüg. A.,' xxiv, p. 441.

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* Literature. The fundamental researches of R. Bright are to be found in his 'Report on Medical Cases,' London, 1827; 'Guy's Hospital Reports,' 1836, 1840. Cf. further: Reinhardt, 'Charité-Annalen,' i, 1850; Frerichs, 'D. Bright'sche Nierenkrankheit,' Braunschweig, 1851; Johnson, 'D. Krankheiten d. Nieren,' trans. by Schütze,' Quedlinburg, 1854; T. Grainger Stewart, 'A Pract. Treatise on Bright's Diseases of the Kidneys,' 2 edit., Edinburgh, 1871. Cf. also the well-known text-books on renal diseases, and works by Rosenstein, 'D. Pathologie u. Therapie d. Nierenkrankheiten,' 2 Auf., Berlin, 1870; by Bartels, in Ziemssen's 'Handb.,' ix, 1, Leipsig, 1875; in the 3rd ed., revised by E. Wagner, 'D. Morbus Brightii,' Leipsig, 1882. An extremely rich source of information is Traube's 'Gesammelte Abhandlungen.'

CHAPTER IV.

COUNTER-PRESSURE.

Experimental evidence as to the importance of the counter-pressure in the secretion of urine.—Morbid impediments in the urinary tubules, the pelvis of the kidney and the ureters.—Malformations of the ureters.—Spastic stenosis of the ureters.—Impediments in the bladder.—Consequences of ligature of the ureters.—Hydronephrosis.—Causes of extreme hydronephrosis.—Hydronephrotic atrophy.

The evacuation of the urine in presence of obstacles in the urinary passages.—Unilateral and bilateral hydronephrosis.

In all the foregoing discussions, it was implicitly assumed that the escape of the urine secreted was perfectly free, and that consequently the secretion-pressure was nowhere opposed by counter-pressure. Yet pathology reveals a great number of conditions, in which the efflux of urine from the kidney is more or less impeded, the obstacle opposing it being sometimes absolutely insurmountable. With these conditions we have now to deal, since the presence of such impediments essentially affects the process of secretion. That this is actually the case, we learn from the researches carried out in Ludwig's laboratory. M. Herrmann* has found that, when such a resistance is present, *the quantity of urine secreted in the unit of time is reduced*, and that there takes place a like *diminution*, but still more pronounced, *in the amount of solid urinary constituents, in particular of urea.* In proportion as the resistance increases, the reduction in volume of the urine and in the contained urea becomes steadily greater, till a period arrives when no urine whatever leaves the kidney. In the dog, this limit is much below the height of the arterial pressure, being 50—60 mm. mercury. So soon, however, as the resistance is done away with, there takes place a very abundant secretion of urine, which is poor in urea and consequently pale and of low specific gravity. These experimental results were, you are aware, regarded by Ludwig as showing that the difference of pressure between the contents of the glomeruli and urinary tubules is the actual cause of the secretion, so that a rise of tension in the tubules must prejudice the secretion of urine, just as does a lowering of arterial blood-pressure. This is not, it is true, a necessary inference from the experiments. Anyone who holds that the velocity of the blood-stream exerts an important influence on the amount of urine secreted, may point to the marked retardation of the flow through the kidneys as explanatory of the reduced secretion when the escape of the urine is impeded. Slowing of the blood-stream has been shown by M. Herrmann to occur during occlusion of the ureter, owing, it is easy to understand, to the pressure exerted by the distended tubules with their stagnant secretion upon the surrounding capillary mesh-work. But the facts above referred to, chiefly fail of being incontrovertible evidence of the pressure-hypothesis, in that they take no account of the *absorption of the urine secreted*. Heidenhain* very fairly reminds us of the absorption of bile, which, you are aware, never fails to take place when its escape is prevented: why an analogous absorption of the urine should not occur, appears the more incomprehensible, as, according to Ludwig's hypothesis, the urine in the interior of the tubules even normally becomes concentrated by absorption. If this be accepted, it immediately follows that the pressure indicated by a manometer, introduced into the ureter, will gradually become less and less till it finally disappears, obviously not because the secretion decreases and is at last arrested, but simply as an expression of the fact that absorption becomes steadily augmented till it accurately counter-balances the amount of secretion. True, not a drop more urine then enters the ureter but only because that poured out into the commencements of the tubules is completely absorbed during its passage through them. That such absorption actually takes place is most strikingly proved by the fact that, under these circumstances, the kidneys become extremely *œdematous.* Not only are the tubules in the kidneys with ligatured ureters tensely filled with secretion as far up as the tubuli contorti, but all the lymphatics of the organ, and even the capsule, as well as the loose fat and cellular tissue surrounding the capsule, are copiously infiltrated with fluid.* To regard this œdema as being merely due to mechanical hyperæmia, does not appear to me justifiable; for though the venous efflux from such kidneys is, it is true, impeded, the impediment cannot, in view of the marked pallor of the organ, be so considerable as would be required to explain such pronounced œdema, from which, moreover, red blood-corpuscles are almost completely absent. Hence, it appears to me much more plausible to look upon the œdema of the kidneys as due to the absorption of the stagnant urine; and at any rate it completely accords with this hypothesis that the œdema disappears on the removal of the counter-pressure, while the excretion of urine becomes for a time almost profuse. All the stagnant and absorbed urine is first evacuated; but in addition, owing to the disencumbrance of the organ, an *arterial fluxion* to the glomeruli can hardly fail to set in at least temporarily, with the result, of course, that an abundance of watery urine will be excreted.

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* M. Herrmann, 'Wien. akad. Sitzgsb.,' Math.-naturw. Cl. (1859), xxxvi, p. 348 (1861); xlv, p. 317.

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* Heidenhain, 'Bresl. ärztl. Zeitschr.,' 1879, No. 22; in Hermann's 'Handb. d. Physiol.,' v, 1, p. 328, *et seq.*

Now whatever may be the situation of the *impediment in the urinary passages*, the abnormal tension will always be transmitted to the commencements of the urinary tubules, *i. e.* to Bowman's capsules; but how great a portion of the secreting apparatus will be affected must depend on the spot at which the resistance is interpolated. An obstacle which occupies a convoluted tube or a Henle's loop simply acts backwards in this individual tube, while if a collecting tube be obstructed, all the branches entering it are involved. If one of the calices be narrowed or occluded, all the tubules of the corresponding section of the kidney will be implicated; and an obstacle seated in any part of the ureter will exert its influence upon the entire organ. That both kidneys may be involved, both ureters must be encroached upon, or an obstacle must be present in the bladder or still further forwards in the direction of the urinary stream. As regards the tubules, in the first place, we have already considered one variety of impediment, which fortunately affects only those of the cortex, *i. e.* their narrowing or complete constriction by *contracting bands of connective tissue;* on the same occasion I also referred to the resulting *cysts,* which are so regularly found in granular kidneys. Tubules altered in this way are, of course, useless so far as the renal function is concerned, yet for this very reason their existence is not betrayed by any change in the urine. This cannot happen unless large numbers, more especially of collecting tubules be occluded. Now it is extremely common to find at the post-mortem the open tubules, in particular, blocked for a longer or shorter distance by a great variety of casts, hyaline and granular, fatty and waxy, hæmoglobin- and blood-casts; and not a few pathologists attribute most severe disturbance of the renal function to their presence. Nevertheless, I cannot, as I have often told you, subscribe to this view; for, in my opinion, all these casts only remain seated in such quantity in the tubules when the secretion of urine is scanty; an abundant secretion readily washes them out of the organ. In order that plugging of the urinary tubules may give rise to a serious impediment to the urinary secretion, the masses must of necessity be solid and unyielding, such, *e. g.* as the *calcareous concretions* which in Litten's kidneys (cf. vol. iii, p. 1166) originated in the dead epithelium. With these, it is true, the pathological *concretions* observed in human kidneys, whether consisting of bile-pigment, urates, lime, or other substance, cannot compare in point of size. When they become very bulky in a short time, as do the *bilirubin-infarcts* in severe icterus of the new-born, the *uric acid infarcts,* also of the newborn, and sometimes too of the gouty, the deposits of *crystalline oxalate of lime* occasionally seen in poisoning with oxalic acid,* they may constitute temporary impediments to the escape of the urine secreted, especially if they are associated with a lowering of the blood-pressure. So soon, however, as the secretion becomes abundant, they, also, yield before the pressure of the stream of urine, and are washed out of the urinary passages. It need hardly be added that cloudy swelling and fatty degeneration of the tubular epithelium can never cause even the slightest resistance to the passage of the urine.

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* Ludwig, 'Wien. akad. Sitzgsber.,' Math.-naturw. Cl., xlviii, Nov. 5th, 1863.

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* A. Fränkel, 'Ztsch. f. klin. Med.,' ii, p. 664. Cf. also Kobert u. Küssner, 'Virch. A.,' lxxviii, p. 209.

In the *pelvis of the kidney*, the escape of the urine may, in the first place, be impeded by *stones*. The chemical composition of the calculi—whose mode of origin will presently be discussed at length—is naturally much less important in this respect than are their form and situation. They sometimes reach a really astonishing size, and may yet prove no essential hindrance to the discharge of urine, except temporarily when they come to lie in front of the orifice of the ureter. More importance attaches to the stones—to be found in every moderately large collection—which form an actual anatomical cast of the pelvis and some of the calices, in which they were firmly wedged. Still, should the secretion-pressure be high, urine will, as a rule, trickle through between them and the wall of the pelvis and calices. Hence, decidedly the most important stones are those, often of no great size, which have become wedged in the funnel formed by the passage of the pelvis into the ureter, or in the commencement of the ureter itself. The occlusion may also be caused by a stone driven on into any part of the ureter, down to the point where this enters the bladder. Moreover, if the stone itself do not constitute an obstacle to the flow, it may cause obstruction in another way, namely, by the ulcerative processes set up, and the consecutive *cicatricial stenosis* of the pelvis and ureter. Obviously, similar strictures may result from ulceration depending on other causes, more especially diphtheritic inflammation. It may happen, furthermore, that other substances, also derived from the kidney or pelvis, will become impacted in the ureter and render it quite impassable, *e. g.* large-sized *blood-clots* and parts of the *cyst-wall of echinococcus*, the latter, it is true, only in very rare cases. Abnormal resistances depending on the presence of tumours are much more frequent, however. It is principally the ureter that is liable to be narrowed or rendered impassable by tumours, which either press it flat, occlude it by growing round it, or, if malignant, directly block its lumen by growing into it. Tumours of all kinds, extra-peritoneal myomas of the ligamentum latum, enchondromas and osteomas of the pelvis, sarcomas of the retro-peritoneal and pelvic lymphatic glands have sometimes been observed to be connected in this way with the ureters, but none of these proves so often prejudicial to the evacuation of the urine as *carcinoma* of the pelvic region, and above all *cancer of the uterus*. True, it is principally the *pelvic lymphatic glands* that here too, when infiltrated by the cancer, narrow or occlude the ureter.

We have not yet, however, exhausted the factors which may make it difficult for the urine to reach the bladder. In the female pelvis, inflammatory processes ending in contraction, *parametritis* and *peritonitis*, may sometimes involve the ureter and cause its constriction. In large prolapses of the vagina where the bladder is also engaged, the entrance of the urine into the latter is often seriously impeded. You remember, further, a case to which I recently referred (vol. iii, p. 1194)—that of a rachitic boy in whom the enormously dilated rectum compressed the ureters as they entered the greatly contracted pelvis. Lastly, some interesting *malformations* play an important part in this domain. I refer to the much discussed, but extremely rare, presence of *valves* in the ureter, as well as to the *abnormal insertion of the ureter into the pelvis of the kidney*. Instead of starting, as it usually does, from the deepest portion of the pelvis, it originates further up, so that in the erect position the urine cannot escape till the pelvis of the kidney has been filled to the level of the origin of the ureter. That we have not in these cases to deal, as has been supposed, with originally double ureters, one of which had subsequently become obliterated and disappeared, is proved by the fact that where two ureters exist, two pelves are also present, which only very exceptionally coalesce the one with the other. We do not know why the insertion of the ureter into the pelvis of the kidney is occasionally abnormal, and it is, as a rule, impossible to discover anything of a certain character from the anatomical preparation, because the ectasis of the pelvis which inevitably sets in under these circumstances, and sometimes assumes enormous proportions, has completely altered the original relations. We sometimes, moreover, meet with sudden bends in the course of the ureter, which must be looked upon as congenital if no fibrous adhesions or bands of connective tissue be present in the immediate vicinity; in some cases observed by us, an abnormal artery crossed the bend transversely, the ureter curving round it. To the same category belong certain malformations of the lower end of the ureter. Passing over congenital atresia, it may occasionally happen that the ureter misses the urinary bladder and opens in a false position, *e. g.* into the urethra, and in woman into the vagina also. Of these, the most interesting from our point of view is the opening of the ureter into the colliculus seminalis, because in this case the termination of the ureter must pass through the muscular prostate, which will involve a considerable obstacle to the regular evacuation of the urine. These malformations appear specially remarkable when conjoined with *double* ureters; for it has then been occasionally observed that one of these double ureters passed through the prostate, while the other entered the bladder in its normal position;* and though complete doubling of the ureter does not give rise to the least disturbance of function if the tubes enter the bladder in normal fashion, here the effects of stagnation of the urine do not fail to set in in the section of the kidney whose pyramids pour their urine into the malformed ureter. For the rest, every such abnormality in the ureter may impede the evacuation of the urine, quite independently of the action of the prostatic musculature, when its orifice is narrower than the normal opening into the bladder.

Whether, in addition to all these "organic" stenoses of the ureter, other so-called "spastic" stenoses occur, *i. e.* such as are conditioned by a tonic contraction of the musculature of the ureter, does not appear to me to be as yet certainly established. I refer of course to lasting stenoses, for I can readily believe that transitory spastic contractions may be set up, owing, for example, to the irritation of pointed and jagged calculi. The question has been raised in consequence of certain cases,† more than once observed, where, owing to unilateral obstruction of the kidney or ureter, a very striking diminution of the urinary secretion, in all other respects normal, or even complete *anuria*, has set in and persisted for some days. Bartels* has also reported a case of complete anuria of more than five days' duration, that of a robust man who had previously suffered from repeated attacks of renal colic, and who about six weeks after the anuria discharged a single stone the size of a bean. It is highly improbable that calculi should in this individual have become simultaneously impacted in both ureters, and that one of them should have subsequently escaped detection, though, on the other hand, it is not certain that he possessed two secreting kidneys. But if in all these cases the anatomical relations were perfectly normal, there is much that is plausible in the view of Bartels, who believes that a reflex inhibition of the urinary secretion —started perhaps by an impulse originating in the one ureter—had occurred. If so, it would still have to be considered whether the suppression was due to a contraction of the ureters or of the small renal arteries, either of which, though possible, would be remarkable enough in view of the persistency of the spasm.

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* Cf. Weigert, 'Virch. A.,' lxx, p. 490.

† Cf. Schmidt's 'Jahrbücher,' 1877, Bd. 176, p. 163.

The passage of the urine from the ureter into the bladder may also be impeded by pathological processes occurring in the latter. We have here to consider, in the first place, *tumours*, benign and malignant, it being immaterial whether they originate in the wall of the bladder or involve the organ secondarily by extension from the uterus or vagina. The effect of such tumours on the evacuation of the urine will be determined essentially by their situation. Very large tumours of the vertex of the bladder need not in the least interfere with the filling of its cavity from the ureters, while small growths even, that have established themselves on the trigone, may cause extreme narrowing or complete occlusion of one or, under certain circumstances, of both ureters. Moreover, that both orifices may at the same time be occluded by a large *vesical calculus* has been shown by an example recently cited; it is probable that small stones do not obstruct the flow from a ureter except when its orifice opens into a diverticulum which is occupied by the stone. On the other hand, nothing is commoner than that calculi of every size should come to lie in front of the internal orifice of the ureter, and so render the emptying of the bladder impossible for a time. Amongst other abnormal resistances which obstruct the passage of the urine in front of the bladder, I may mention as the most frequent and consequently important kinds, pathological *enlargements of the prostate*, in particular so-called prostatic hypertrophy, and *strictures of the urethra*.

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* Bartels, in Ziemssen's 'Handb.,' ix, 1, p. 44; Ingw. Paulsen, 'Bemerkungen und Versuche zur Lehre von der Nierenthätigkeit,' Inaug.-Dissert., Kiel, 1871.

To these last-mentioned factors we shall shortly have to refer at greater length; they have been mentioned here chiefly for the sake of completeness. For it would be an error to suppose that every process impeding the evacuation of the urine at once makes its influence felt as far back as the kidneys. This is prevented by the interpolation between the obstacle and the kidneys of a capacious and at any rate extremely distensible reservoir, the urinary bladder. The kidneys and their function will be affected by resistances situated in front of the bladder only *when the organ is unable to overcome these resistances*; then, however, they will certainly be influenced, because the condition is in all essentials identical with a direct impediment in the ureters.

In now seeking to understand the effects which an obstacle opposing the escape of urine exerts on the renal function, it will be our simplest plan to first fix our attention on the consequences of *sudden and complete occlusion of one of the ureters*. We have not infrequently an opportunity of observing such occlusion in man as the result of the impaction of a renal calculus in some portion of the ureter, and with its effects we are thoroughly acquainted, since nothing is easier than its production by *ligaturing one of the ureters* in a rabbit or dog; the connection of a mercurial manometer endways with the ureter also involves complete occlusion after a short time. Now, you already know what happens. At first the urine flows as usual from the papillæ into the pelvis of the kidney; the flow then begins gradually to diminish as the pelvis and pervious part of the ureter become filled; and, finally, it ceases completely when the tension in the pelvis has reached a certain level, which varies for different species and for different individuals of the same species, as well as in correspondence to the energy of the secretion, but in the dog averages about 50 to 60 mm. mercury. The pelvis of the kidney and the section of the ureter above the ligature are now strongly distended and filled to their utmost capacity with urine. The time elapsing before this occurs naturally varies extremely, according to the roominess of the parts concerned and the activity of the secretion at the moment of closure ; still we need never wait long before the further flow ceases completely. The setting in of absorption of the urine now very soon begins to be recognisable from the evident *œdema ;* owing to this the volume of the kidney is considerably augmented, and even the perinephritic fat becomes thoroughly moistened, while the lymphatics of the hilus are seen to be distended and filled with a clear fluid. Yet this is not all. If the urinary organs of the animal be examined six or eight hours after the ligature of the ureter, or still better on the following day, more or less copious hæmorrhages are found in the fatty capsule, in the wall of the renal pelvis and fat surrounding it, but mainly throughout the entire wall of the intensely red ureter right down to the ligatured spot. These hæmorrhages never fail to set in, even when particular attention has been paid to cleanliness and the operation has been carried out antiseptically, and are, according to my experience, relatively more marked in the rabbit than in the dog. I must not conceal from you that the source and origin of these hæmorrhages are not perfectly clear to me ; it is most probable however, that they are due to mechanical hyperæmia, depending on the compression of some of the veins by the overfilled urinary passages ; at any rate, it perfectly agrees with this explanation that after a few days, *i. e.* so soon as a sufficient number of effluents are provided for the escape of the stagnant blood, the redness of the ureter and soon afterwards the bleedings have usually disappeared. The contents of the pelvis of the kidney and ureter are what might be expected from the existing conditions. At the time when the hæmorrhages are most abundant, large numbers of red blood-corpuscles and often small clots are found in the fluid filling the ureter ; but if this be allowed to escape and a fresh ligature be applied immediately, the fluid is found after a few days to be perfectly clear, pale, and practically free from blood-corpuscles. As was long ago shown by Ludwig, the mechanical hyperæmia extends as far as the kidney, and to this hyperæmia it is most certainly due that a small quantity of *albumen* and a few hyaline *casts* are contained in the urine secreted by a kidney after the removal from the ureter of a ligature which had been applied for twenty-four hours previously. In rabbits I have never failed to find such casts in the urine, and they are also regularly discovered inside the urinary tubules of the animals killed during the first few days after ligature of the ureter; in dogs, on the other hand, they cannot be so certainly counted on, apparently because a larger number of more capacious effluents remain open in these animals,—a circumstance which in itself is enough to overthrow the strange and sweeping conclusions which Aufrecht* has drawn from the occurrence of these casts. For the rest, the absence of casts from the kidney of the rabbit after the sixth day, has not escaped the notice of this writer also.

Meanwhile, the condition of the pelvis of the kidney and of the portion of the ureter above the ligature has not remained unchanged, *the distension of these parts having undergone a gradual increase.* Unlike the case of hydrops cystidis felleæ, it is here, in my opinion, unnecessary to have recourse to a continued secretion by the mucous membrane of the pelvis in order to explain the increase of volume. The pelvis of the kidney is not surrounded on all sides by closed walls, but communicates freely with the kidney, which on its part has by no means ceased to secrete. If it be owing solely to the high tension under which the contents of the pelvis are placed that not a drop more urine enters its cavity, the flow should at once recommence so soon as the tension is reduced. And it will be reduced, inasmuch as the wall of the pelvis and ureter gradually yield before the pressure to which they are continually subject. Hence it is easy to understand that, during the next few weeks, a very considerable *dilatation of the ureter and pelvis of the kidney* is developed, *i. e.* a condition which, you are aware, is termed hydronephrosis by the pathological anatomist. The fluid contained in the dilated pelvis is a very thin watery solution of urinary ingredients with a little albumen; its formed constituents are extremely few, though the number of pus-corpuscles may become very great, if, during the operation of ligature, exciters of inflammation have found their way into the urinary passages shut off, and have given rise to a purulent pyelitis or pyelonephritis. The contents of such a *pyonephrosis* will also of course be richer in albumen. But if you ask, what finally becomes of a kidney whose ureter remains permanently ligatured, I reply that, according to my experience, the end-result will not be more than a *moderate* degree of hydronephrosis. This appears to me to be due to the fact that, in consequence of the permanent high tension in the pelvis, the circulation through the kidney gradually suffers,—first, of course, in the papillæ or sections of the pyramids embraced by the calices, but ultimately in the upper parts of the pyramids and cortex also, especially in the septa Bertini, the latter effect being due to the pressure exerted upon the vessels as they enter the kidney in the vicinity of the pelvis. Proof of the obstruction of the circulation is afforded, in the first place, by the *flattening of the papillæ* which takes place *pari passu* with the gradual enlargement of the calices, and, in the next place, by the constant presence of *anæmia* of the entire kidney. At the same time, you will note that the pale organ is no longer œdematous as at first, but even conspicuously dry,—striking proof that the mechanical hyperæmia and the urinary secretion are both at an end.

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* Aufrecht, 'Med. Centralb.,' 1879, p. 337.

The examples of really voluminous hydronephrosis are, in fact, never due to rapid complete closure of the ureter; they arise only when the *occlusion is very slowly developed* or in extreme narrowing which yet leaves a portion of the lumen free, or when the resistance is *not permanent but alternates with periods of perviousness.* Very extreme hydronephrosis may be experimentally produced in the rabbit, and still better in the dog, by *loosely* surrounding some part of the ureter by a carbolised thread, which must not be too thin. There develops around the thread a circumscribed non-suppurative inflammation, leading to the formation of a fibrous capsule which by gradually contracting narrows the ureter. In man the occurrence of slow occlusion is most commonly due to tumours which grow round or into the ureter. Narrowing is met with in its most pronounced form where *cicatricial strictures* exist or when *valves* are present in the ureter; the latter, even when directed upwards, do not usually completely obstruct the lumen of the tube. Lastly, the alternation of occlusion with perviousness of the ureter may be most simply brought about by the repeated impaction and loosening of calculi: yet it is obvious that this injurious succession can only rarely be repeated in the same kidney with the necessary constancy, and hence *bends* and *faulty insertions* of the ureter into the pelvis of the kidney afford the most fruitful examples. When, for example, the ureter springs from the upper part of the pelvis, it will be impossible, as already stated, for the urine to enter it, while the body is in the erect position, until the pelvis has been filled to the level of the ureter. Now the pelvis is bounded by a yielding and distensible wall which will gradually dilate under the influence of the accumulated urine, till the size of the sac when full allows of its completely compressing the ureter which lies upon the pelvis as it passes downwards. Only in the erect position, however; for when the owner of such a kidney lies down, *e. g.* during sleep, the urine is unopposed and flows uninterruptedly from the sac into the urinary bladder. In bending of the ureter, on the other hand, the alternation is secured by a sort of elevation of the section of the ureter lying above the bend, which takes place as the tension increases, so that the bent portion now resembles the junction of the conical part of a funnel with the neck; the greater part of the urine can thus flow away, whereupon the bend is re-established at its original situation. But even in cases of simple narrowing the impediment to the excretion of urine is far from being always the same, however little the resistance itself may vary. Supposing a considerable narrowing to have occurred during a period of copious secretion, a moment will comparatively soon arrive, though not so rapidly as if the obstruction were complete, when, owing to the disproportion between afflux and efflux, the pelvis and proximal part of the ureter will be so full and tense that no more urine can enter from the kidney. Soon, however, the pelvis rids itself of its excessive contents, which flow away through the narrow spot partly in obedience to gravity and partly with the aid of the energetic peristaltic movements of the musculature of the ureter, which is abnormally excited by the resistance; whereupon the cycle begins afresh. It is obvious without further discussion that no such marked alternations between excessive fulness and absolute emptiness of the pelvis can in reality occur; but this circumstance clearly makes no difference in principle. For it is solely owing to this mechanism that the kidney retains the power, after a longer or shorter interval during which the escape of the urine is interrupted, of *again discharging considerable quantities into the pelvis;* and this is possible not only in the first-named malformations but in narrowing also, and since, in gradual occlusion of the ureter, the final closure is necessarily preceded by a long stage of partial obstruction, it will be possible in cases of this category as well.

Why this particular condition of affairs should prove so favorable to the development of voluminous hydronephrosis is evident without further discussion; the secretion of the affected kidney is never completely and permanently suppressed, and consequently more fluid enters the pelvis than if the ureter were completely occluded. It is, however, to one circumstance more particularly that the accumulation of a great profusion of fluid in the accessible urinary passages is due—namely, *the behaviour of the renal secretion after the removal of the abnormal resistances.* When the obstacle opposing the escape of the urine disappears, and the glomeruli are in consequence relieved from the counter-pressure acting upon them, there immediately takes place *a copious secretion of very light and clear urine.* This is the reason that, in persons in whom the insertion of the ureter is abnormal, such a considerable quantity of urine enters the bladder so long as they remain lying, and can therefore be evacuated; while if the passage to the bladder is not perfectly free, as in the case of the same individuals when they stand or walk, or in stenosis of the ureter, the result of the profuse secretion is that the pelvis and ureter are always filled with large quantities of urine and excessively distended. And because, so long as the efflux from the overfilled pelvis is at all possible, the urinary secretion never ceases, the process may be repeated for years, and tens of years in the same identical fashion, though not, it is true, without gradually bringing about a *really enormous dilation* of the parts in question. Even the hydronephrosis due to compression by tumours usually considerably exceeds in dimensions the variety produced by sudden occlusion of the ureter; yet the narrowing is here, as a rule, too rapidly converted into closure, and, owing to the disease at the bottom of it, does not usually last long enough to allow of the production of really extreme hydronephrosis. The colossal hydronephrotic sacs which have repeatedly been mistaken for large ovarian tumours and sometimes reach the size of a man's head, are met with as the result of cicatricial strictures, and more particularly in cases where the ureter is abnormally inserted, or bent, or contains valves,—malformations, that is, in which sufficient time is allowed for the development of such enormous ectasis. The proximal section of the ureter may then acquire the thickness of a loop of small intestine, while the hydronephrotic sac itself has so little resemblance to the normal pelvis renalis that an immediate diagnosis is often only possible through recognising, on the circumference of the sac, the greatly dilated calices, which communicate with the main cavity by large neck-like openings. At any rate, these secondary sacs form a much more striking characteristic of the large hydronephroses than does the renal substance enveloping the sac. The latter is in these cases extremely thin, and appears in many places to be completely absent: in most it scarcely measures more than one or two millimètres in thickness, and if thicker portions are present at all, they are seated on some isolated part of the periphery which can only be discovered by careful dissection on every side. Now it must not be forgotten that a layer of renal tissue of only a millimètre in thickness may, since it surrounds the enormous sac, be approximately equal in bulk to a mass ten or twenty times as thick arranged around the normal pelvis; what has taken place is a very considerable extension of superficies, naturally at the expense of the thickness of the kidney. Nevertheless it is undoubtedly correct to speak here of hydronephrotic atrophy. The pyramids are invariably absent, and even in the still remaining cortical portion we often meet with that increase of the interstitial tissues which affords striking testimony to the loss of epithelium and obliteration of the urinary tubules. The glomeruli, more especially of the outer layers of the cortex, are best and longest preserved, as you yourselves have doubtless inferred from the continuance of the urinary secretion so often referred to. The contents of these large hydronephrotic sacs must necessarily be *urine*, provided the efflux is still possible and a permanent stagnation of the fluid has not yet taken place. This urine will be very watery, it is true, and as a rule, though not always, contains *small quantities of albumen*, but no casts, and scarcely any other formed constituents, unless, indeed the hydronephrosis is complicated with inflammation, hæmorrhage, or other pathological process. Kehrer* once observed an abundant development of gas, chiefly carbonic acid, in the interior of such a hydronephrotic sac.

Contrasting with the effects just discussed, which are exerted on the kidney and its function by the rise of counter-pressure depending on the interpolation of a resistance in the urinary passages, we have now to consider the results of an opposite kind and to examine how the *discharge of the urine* is affected in persons with such resistances. It need hardly be said that when the ureter is completely occluded not a drop more urine can enter the bladder from the corresponding kidney or be discharged from the body. Hence the inevitable consequence of the closure of both ureters is the production of an *anuria* no less complete than that which ensues when a stone blocks the opening of the urethra, or a prostatic tumour or very tight stricture occludes some portion of its lumen. The anuria continues as long as the closure of the urinary passages persists, and when the impediment is not removed, either spontaneously or artificially, there set in sooner or later, but always in a very short time, the phenomena shortly to be discussed which attend the retention of urinary constituents in the organism and are known in pathology as "uræmic"—phenomena whose regular termination in these cases is death. When, on the contrary, the impediment is got rid of, there follows, in harmony with the oft-mentioned results of experiment, *an extremely abundant and*

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* Kehrer, 'Arch. f. Gynäkolog.,' xviii, Hft. 3.

profuse excretion of very watery and light clear urine, which usually contains small quantities of albumen. Thus Bartels found that the patient already referred to evacuated more than 3300 c.c. urine during the first twenty-four hours after the passages had become pervious on the removal of the impacted stone and relaxation of the spasm of the other ureter. Similarly, it is an old experience of the surgeon that men who, owing to stricture of the urethra, pass no urine for several days, discharge during the next twenty-four to forty-eight hours after catheterisation enormous quantities of very dilute secretion.

Nothing of this kind is observed, however, when only one kidney or a portion of one is shut off from the urinary bladder. The kidney, or the portion involved, sends no urine into the bladder, it is true; still the quantity secreted by it and immediately absorbed will be so readily and perfectly excreted by the other kidney, or by the pervious portion of the partially occluded one, that no diminution in the volume of the urine sets in. If one of the ureters be tied in a dog and no inflammation or disturbance of the animal's general state follows the operation, the amount and constitution of the urine will remain unaltered if the diet be the same as before. And this will be the case not only during the first few days and weeks after the operation, but later also, when the affected kidney undergoes hydronephrotic atrophy, becomes anæmic, and ceases to secrete. For there is meanwhile developed a *compensatory hypertrophy* of the second kidney, which is now capable of meeting the demands originally made on both kidneys together.

Moreover, when, instead of a unilateral occlusion of the ureter, we have to deal only with narrowing on one side, or with one of the malformations which give rise to a periodical alternation of closure with perviousness of one of the ureters, the urine does not usually betray the presence of the lesion by any characteristic sign. The second kidney with normal passages is always ready to compensate for any disturbance that may occur in the secretion of the opposite organ; and consequently you need feel no surprise should you find, in the history even of very large unilateral hydronephrosis, abundant reference to the various symptoms usually attending enormous abdominal tumours but nothing of a noteworthy character as regards the urinary secretion. You must be prepared, however, for an abnormality of the urine in *bilateral* lesions of this kind. Narrowing of both ureters, unless very slight, leads to *a diminution of the volume of the urine and of the urea-contents,* while extreme stenosis is attended by such a degree of oliguria that a fatal retention of urinary constituents takes place, though less rapidly, it is true, than when the occlusion of the ureters is complete. The greatest interest attaches, lastly, to the bilateral hydronephroses which arise in consequence of *intermittent* occlusion of the ureters, not so much owing to the fact that they present the most extreme degrees of this affection, as because the interruptions to the impediment are clearly reflected by the urinary secretion. For in these cases, *periods of oliguria and complete anuria alternate with marked polyuria.* The frequency of the alternations and the intervals at which they take place vary, indeed, extremely, and depend above all things on the nature of the impediment. In the case of a woman with bilateral abnormal insertion of the ureters into the pelves in which I made the post-mortem examination, the patient had for a long time passed practically no urine during the day, but had produced very considerable quantities during the night. Yet such regular alternations will occur only rarely, if for no other reason because the secretion cannot be relied upon to proceed on both sides in precisely the same fashion. Sometimes an anuria lasting several days is followed by a period equally long of very pronounced polyuria, and this again by an interval during which the volume of the urine continues great, but without markedly exceeding the normal; it is only necessary for the anuric period of one kidney to coincide with the polyuric period of the other, or for anuria and polyuria to alternate several times during the same day, in order that on the whole the urinary secretion may be approximately normal. Still more if it be temporarily impacted stones that occlude the ureters for a time, or a large but movable vesical calculus that now and then gets in front of the orifices of both ureters, or a dilated rectum that compresses both ureters only when it is full, the occurrence of a regular alternation of anuria with polyuria will be altogether out of the question. Why it is that under these circumstances the excretion of urine so often exceeds the normal amount, you are aware already; this is, in the first place, the direct result of each disappearance of the resistance; and in the second place, it is precisely in these hydronephroses that *a rise of arterial pressure and cardiac hypertrophy* are most readily developed, provided the affected individuals are still young and in other respects healthy and vigorous. In the really large forms, it is true, the resulting digestive and respiratory troubles, &c., will be attended by general constitutional disturbance; yet you no doubt remember that the examples of hydronephrosis which I myself adduced (vol. iii, p. 1194) were cases of the last category with only temporary occlusion of the ureter. When, however, a regular hypertrophy of the heart has once been developed, the urinary secretion is not only abundant during the period immediately following the removal of the abnormal resistance, but remains so as long as the urinary passages continue pervious and easily passable.

CHAPTER V.

THE URINARY PASSAGES.

Solutions of continuity in the walls of the urinary passages.—Their causes and consequences.—Urinary fistulæ.

Changes in the urine produced by pathological products in the urinary passages.—Alkaline fermentation of the urine.—Its causes and consequences.

Concretions in the urine.—Acid fermentation of the urine.— Uric acid stones.—Their formation.—Oxaluria and oxalic acid concretions.—Phosphatic calculi.—Vesical calculi.

Normal evacuation of the urine.—Its derangements.—Tenesmus ad matulam.—Impediments to the emptying of the bladder, and their effects.—Retention of urine.—Incontinentia urinæ.—Ischuria paradoxa.

In the brief remarks with which I introduced the pathology of the urinary organs, I reminded you that the urine does not at once leave the body when secreted, and that it is more necessary in the case of the kidneys than of any other gland to clearly distinguish between *secretion* and *discharge.* In other words, the *secretion* of the urine may be normal, and yet the urine *evacuated* may be abnormal. Now we have just thoroughly discussed perhaps the most important group of disturbances of evacuation,—the presence of impediments in the passages and the resulting interference with the escape of the urine; we were compelled to anticipate matters because, as you saw, these disturbances have an important effect, not merely on the evacuation of the urine, but on the process of secretion itself. Even assuming, however, that the urinary passages are everywhere pervious, and the channel free from pedime [illegible] rine passed [illegible] the urethra may nevertheless differ in amount and constitution from the pure secretion. Several other conditions must be fulfilled, and we shall begin by considering one with which you are familiar in connection with the various other cavities and passages of the body, namely, *the necessity that no other opening but the normal ones should be present in the wall of the urinary passages.*

Solutions of continuity in the wall of the urinary passages are very far from rare, and may occasionally be observed in any one of its parts. Their causes are identical with those which we found gave rise to perforations of the bile-passages and other canals, namely, *traumata* and *ulcerative processes.* An incised or bullet-wound may pierce any portion of the urinary passages, the pelvis of the kidney or the bladder, the ureter or urethra, the wound being often enough associated with injury to other parts, which adds considerably to the importance of the trauma. Owing to the application of a diffused force, or in consequence of a fall on a hard object, the urethra or bladder may be lacerated, sometimes indirectly as the result of fractures of the pelvic bones. Surgical errors, moreover, play a not unimportant part in the ætiology of such perforations. Thus the forcible introduction of a catheter or sound may cause a so-called *false passage* in the urethra, or, if the bladder be paralysed and non-sensitive, may lead to direct perforation of its wall in the region of the vertex. Perforation of the bladder may also occur during operations upon it, and still more frequently during obstetrical practice: even the ureters have repeatedly been incised during obstetrical and gynæcological operations, *e.g.* ovariotomy. Amongst the ulcerative processes, those produced by *stones* are by far the most numerous. It is here certainly the very rare exception for a pointed or jagged concretion to directly perforate a ureter in which it is impacted; the almost invariable course of events is the production by the pressure of the calculus of a necrosis with secondary inflammation, under the influence of which the rupture ensues. This process has also been observed in the pelvis of the kidney as well as the ureter, further in the urinary bladder and even the urethra,—in short, in every part of the urinary passages, since, as you will presently hear, stones may become wedged in all these places.

The perforations arising in consequence of other ulcerative processes are much rarer than those which are occasioned by calculi—that is, if we leave out of account the *cancerous* communications of the bladder with the rectum, and more especially with the vagina and uterus, which, unfortunately, are only too frequently observed by the physician and anatomist. Now wherever an apparently spontaneous rupture has occurred in some portion of the urinary passages, you will never omit to explore the part for the ulcerative process or antecedent trauma; for an otherwise healthy bladder or pelvis never ruptures as the consequence merely of over-distension; the bladder may be enormously dilated owing to an impermeable stricture of the urethra, and may extend high up into the abdominal cavity; the pelvis may be extremely ectatic, and at the same time tensely filled—still you need never fear a rupture, simply because, as you are aware, the urine ceases to flow so soon as the tension on the proximal side of the obstruction has reached a certain elevation. True, it need hardly be said that the bladder, when extremely distended and overfilled, will much more readily be ruptured by a diffused force applied to the abdomen than when contracted or only partially filled.

Apertures in the urinary passages are in very bad repute with the public, and for good reasons; for only too often they run a dangerous course. Still the danger should not be exaggerated. The urine is a fluid destined for removal from the body, and should it escape from the passages through an abnormal opening, this never involves any loss to the organism; on the other hand, normal urine is not at all an injurious fluid, so that contact with it is not attended by prejudice to the organs and tissues generally. If you divide the ureter of a dog in the abdominal cavity at a distance of a few centimètres from the bladder, no noteworthy disturbance takes place, provided a traumatic peritonitis be averted; for the urine which at first freely enters the abdominal cavity is at once absorbed and then excreted by the other kidney. This state of things does not last long, however; the cut end of the ureter soon begins to contract, and after a time is
und to be closed by cicatricial tissue respond-
g kidney has undergone hydronepl t, per-

forating wounds of the bladder are far from always proving fatal. True, if a widely gaping wound, also involving the peritoneum, is situated in the lower segment of the bladder, it is almost inevitable that the great bulk of the urine should constantly flow away into the abdominal cavity and should thus give rise to a fatal retention of urine. On the other hand, wounds of the vertex by which the evacuation *per urethram* is not prevented, can very well heal. But such a favorable course is taken only when the escaping urine is and continues normal, and the dangerous element in these accidents is the fact that the urine is *a very readily decomposable fluid.* When the escaped urine comes into contact with certain organisms capable of exciting fermentation—and an opportunity for this is afforded by all kinds of wounds—what is known as *alkaline fermentation of the urine* sets in, of which more anon; and the urine so altered, far from being indifferent to the tissues, gives rise to the most severe necrosive, diphtheritic, and purulent-hæmorrhagic inflammations. But since the urine is often enough in a decomposing state, in the ulcerative processes due to calculi, &c., which initiate the non-traumatic perforations of the urinary passages, while a limited necrotic-purulent inflammation of the wall is also invariably present in addition, these solutions of continuity are under all circumstances more serious than the purely traumatic. The decomposing urine gives rise in the abdomen to a severe and probably always fatal peritonitis; and if the opening be extra-peritoneal, *e. g.* in the posterior wall of the pelvis of the kidney, the result is a very tedious and by no means harmless purulent perinephritis with formation of abscesses. Again it is simply the ease with which the urine decomposes that causes the urinary infiltration of periurethral and pelvic cellular tissues, in consequence of ruptures of the urethra and region of the neck of the bladder, to be so dangerous and so dreaded.

Such being the state of affairs, it is decidedly a piece of good fortune that provision is usually made, more especially in the perforations taking place from within outwards, by antecedent inflammation and the formation of adhesions, against the escape of the urine, together with the stone or other impurity, into the cavity of the abdomen or subperitoneal cellular tissue; with the result that it is directed into *some other communicating cavity*. On the left side, the pelvis of the kidney has been observed to communicate with the colon and with the stomach, on the right with the cæcum and gall-bladder; on both sides ruptures in an outward direction through the lumbar muscles have been seen. The urinary bladder has been repeatedly found in perforative communication with a loop of intestine, with the gall-bladder, and also with the stomach; perforations forward through the abdominal wall, or in the inguinal region, or perineum are far from rare, and I have just referred to the great frequency of recto-vesical and vesico-vaginal fistulæ; the latter, if not traumatic, mostly depend on a cancerous process, yet the calculous perforations also contribute their contingent. Fistulæ of the ureters lead either outwards, or, when due to gynæcological manipulations, into the female genital tract. Fistulæ of the urethra may open in the female into the vagina, while the much more frequent urethral fistulæ of the male may select any portion of the penis or scrotum or even of the neighbouring skin.

While the actual danger to life is averted by these fistulous communications, they are anything but desirable occurrences. They are attended by troublesome disturbances in two different directions. In the first place, it may easily happen, in communications with other cavities, that foreign bodies escape into the urinary passages, and there give rise to inflammation and more especially to the formation of concretions and stones with all their consequences. The second, and, as a rule, much more disagreeable result for the patients arises from their inability to control the escape of the urine from the fistulæ and communicating cavities. True, when the escaping urine enters the intestine, the patient usually succeeds in preventing its constant trickling *per anum*; yet profuse diarrhœa is present, as a rule, in these cases, the motions containing pus and having a urinous odour when, as usually happens, the pelvis of the kidney or the urinary bladder is in a condition of pyelitis or cystitis. In urethral fistulæ, also, the urine, it is evident, will escape in more or less large quantities through the abnormal opening, only when it is voluntarily evacuated *per urethram*. But the state of persons with external fistulæ of the pelves of the kidneys, ureters or bladder is all the more deplorable, and no less lamentable is the condition of a woman with a fistula leading from the bladder or ureter into the vagina. The urine as it trickles away keeps up a continuous eczematous inflammation of the skin or external genitals in the neighbourhood of the fistulous opening; the dress is constantly wet; and the ammoniacal urine gives off a penetrating odour; in short, the situation of these unhappy patients is very often so painful that they willingly consent to the most serious operations, such as closure of the vagina or even extirpation of a kidney, in the hope of securing relief.

The necessary consequence of every abnormal opening in the wall of the urinary passages, however arising, must obviously be a diminution of excretion by the normal channel; for the amount discharged *per urethram* will be less than that secreted, by the quantity escaping through the fistula, &c. For the rest, the urine evacuated *per urethram* as well as that coming from the fistula may be perfectly normal in composition, clear, acid, and without any formed constituents. In the majority of such cases, however, the urine is not qualitatively normal, even when the kidneys have remained free from all pathological processes; and as regards hydronephrosis also, I have, as you will remember, repeatedly dwelt on the fact that a clear, acid urine, which only departs from the normal in amount and urea-contents, is far from being always met with. But such anatomical alterations as stenoses and solutions of continuity are not even necessary to produce an occasional difference in composition of the urine discharged through the urethra and that secreted by the kidneys. In a normal condition no such difference is found, as you know. The urine secreted by the kidneys flows without delay into the bladder, partly by the force of gravity and partly owing to the pressure of the following secretion, but more especially by the aid of the peristaltic contractions of the ureters; and after a longer or shorter stay in the bladder it is discharged from the body by the contraction of the bladder-wall. That a few epithelial cells, and perhaps also some mucus, may become mixed with the urine during its transport is not to be denied, but passing over these harmless impurities, the urine undergoes no alteration between the pelvis of the kidney and the ureter, if its stay in the bladder is not unduly prolonged. This preservation of its original characters by the secreted urine depends, in the first place, on the fact that no secretion is poured out by the wall of the urinary passages and mingled with the urine, so long as the mucous membrane with its epithelium, vessels, glands, &c., are normal in structure and function. And as for absorption, though the normal vesical mucous membrane is capable of absorbing all watery solutions with which it comes into contact,[*] yet it requires a much longer time to effect this than is usually spent by the urine in the bladder; and while the absorptive capacity of the mucous membrane of the urethra considerably exceeds that of the vesical mucous membrane, yet the rapidity of the passage of the urine through the urethra renders all absorption impossible.

On the other hand, we can no longer count upon an unaltered constitution of the urine when the integrity of the mucous membrane has been destroyed owing to pathological causes. I recently told you that when an abnormal communication exists between the urinary passages and other cavities, foreign matters may enter the urine. When bile flows from the gall-bladder into the pelvis of the right kidney or into the urinary bladder, the urine must acquire icteric characters, and it may happen in this way that a gall-stone may be discharged *per urethram* or may form the nucleus of a vesical calculus. But much more extraordinary objects, such as pieces of meat, raisin-stones, &c., may be carried away by the urine as the result of communications with the intestines or even the stomach. These foreign bodies, though sufficiently striking, are decidedly less interesting, however, than true *pathological products*, which have effected an entrance to the urinary passages by perforating the mucous membrane, such, *e. g.* as soft, pulpy, or even cystic tumours, whose contents—fluid fat, hæmatoidin and other crystals,[†] pigmented cells and flakes, in short, all kinds of material—may become mixed with the urine. Shreds and fragments of soft, villous, or disintegrating *carcinomas* of the urinary bladder are also sometimes passed with the urine, but they are seldom sufficiently characteristic to admit of a certain diagnosis. This brings us to the domain of the actual *diseases of the mucous membrane* of the urinary passages, and it is by these that the composition of the urine is by far the most frequently influenced. Many cases of *hæmaturia* depend upon hæmorrhages into the urinary passages, and when a great number of red, but very few colourless corpuscles are present in the sediment, and casts are completely absent, it is much more probable that you have to deal with hæmorrhage from the pelvis of the kidney, ureters, or bladder than with a hæmorrhagic nephritis, and this probability is considerably strengthened when actual blood-clots have escaped with the urine. For the rest, I need hardly say that true hæmorrhage may also take place from the kidney into the pelvis. I may remind you, next, of the *lymph-* and *chyle-fistulæ* opening into the urinary passages, owing to which the urine may acquire a perfectly chylous character (cf. vol. iii, p. 1216). The *inflammations of the mucous membrane* are more important, however. Of these, the most frequent form, suppurative inflammation, has been touched upon on a previous occasion (vol. iii, p. 1208), when I pointed out what a copious sediment of pus-corpuscles is thrown down by the urine in suppurative *pyelitis*. The same thing occurs in acute, and more especially in chronic, *cystitis;* nor is pavement epithelium—easily distinguishable by its form from the epithelium of the tubules—absent in inflammation of the pelvis and bladder. The suppurative pyelitis and cystitis are not uncommonly complicated by a *diphtheritic* inflammation of the mucous membrane of these parts; yet we sometimes also meet with a pure *croupous* inflammation leading to the formation of true fibrinous membranes. This croup of the urinary passages has been observed more particularly after acute poisoning by cantharides, and sometimes extends from the pelvis as far as the bladder; provided the patient survives the first few hours, it usually takes a favorable course, so that the large fibrinous shreds and tubes disappear from the urine after a few days. Lastly, we have here to consider the *tuberculous* and *lympho-sarcomatous* inflammations of the urinary passages, a common feature of which is that they vary greatly in their distribution, being sometimes no more than mere foci of disease in the pelvis or the neck of the bladder, and at other times extending without interruption from the pelvis of the kidney through the entire ureter into the bladder and even the urethra. Since these processes regularly lead to breaking down of the superficial parts, detritus must inevitably enter the urine and be discharged with it; the urinary secretion of these patients is consequently more or less cloudy, and deposits a sediment, although it is perfectly normal in amount, reaction, specific gravity, urea-contents, &c., and need not contain more than minute quantities of albumen. It is generally characteristic of the urine in such cases that in all essential particulars it agrees with the healthy secretion—provided at least that the kidneys are not otherwise diseased. Could we succeed in completely removing the particles of detritus, the masses of fibrin, the epithelial cells, &c., the urine would be found to be perfectly normal, such as would correspond to the general condition and diet of the individual concerned. And this would hold true even of the suppurative and purulent-diphtheritic cystitis and pyelitis, were it not that in the majority of these cases the urine is distinguished in a very marked manner from the normal secretion, *i. e.* by its *neutral* or even *alkaline reaction*.

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[*] Cf. Maas u. Pinner. 'D [illegible] schr. f. Chir.'

[†] Ebstein, 'Deutsc [illegible] Med.,' x

The conditions under which the urine may acquire an alkaline reaction differ greatly in character. When the alkalinity is due to the use of potash, soda, or of the vegetable salts of the alkalies which are converted into carbonates in the body, it is evidently nothing pathological; and if the urine of persons suffering from disease of the stomach, whose gastric juice is deficient in acid and who are accustomed to vomit the greater part of the stomach-contents—if, as I formerly told you (vol. iii, p. 1113), their urine loses its acid reaction, it is not the urinary apparatus that performs its functions abnormally. Not so with the alkalinity of the urine in pyelitis and cystitis. For in these diseases the urine *has its usual acid reaction when secreted, and has only become alkaline within the urinary passages.* This change is effected by the same process which invariably transforms the urine, after its discharge from the body and exposure for a longer or shorter period to the air, into an alkaline fluid, smelling of ammonia, *i. e.* by the so-called *alkaline fermentation.* The latter has long been known to consist essentially in the transformation of urea into *carbonate of ammonia* and the secondary processes following thereupon, as weakening of the acid reaction, separation of oxalate and neutral phosphate of lime, the formation of triple phosphate and of amorphous deposits of urate of ammonia; and no one now doubts that the decomposition is initiated solely by the action of organised ferments, the ubiquitous *torulæ of the urine* or *micrococcus ureæ,* so-called by F. Cohn. But strange to say, the conclusion following therefrom for our organism also has not been unreservedly accepted by a number of pathologists. They do not of course deny the possibility that in the human body stagnant urine may be caused to undergo alkaline fermentation by organisms which have entered it from without; but they maintain at the same time the old and formerly quite comprehensible view, that this fermentation may be brought about by the stagnation, or may develop under the influence of the vesical mucus, shed epithelium, or pus-corpuscles. Yet this opinion is quite untenable. On ligaturing one of the ureters in a dog with the necessary precautions, alkaline fermentation never sets in in the pelvis of the kidney, however long the time allowed to elapse since the application of the ligature; and in man also the urine contained in a hydronephrotic sac may continue clear and acid for many months; in fact, it will do so as a rule, when the ureter is completely and permanently closed, *i. e.* when the stagnation of the urine in the pelvis of the kidney is complete. That the opinion above referred to should nevertheless have arisen, is explained without difficulty by the fact that alkaline fermentation is specially prone to occur when for any reason the urine stagnates in some part of the urinary passages; thus, it readily takes place in hydronephroses, behind strictures of the urethra and tumours of the prostate, and in paretic or paralytic bladders which are not evacuated in a regular manner. Still this preference depends only and solely on the circumstance that the alkaline fermentation, for the development of which outside the body several days are as a rule required, does not, even under the more favorable conditions presented by our organism, set in suddenly, but requires for its production a space of time which is not secured it when the urine is normally passed. I have already mentioned (vol. i, p. 302) that when a liquid containing bacteria is introduced into the bladder of a healthy dog, no reaction is set up, simply because the schizomycetes are removed with the urine next evacuated. But if immediately on injecting the fluid, a ligature be firmly tied round the penis, it will soon be found—certainly within a few days—that the urine of the bladder is neutral or even alkaline, *i. e.* in a condition of alkaline fermentation. A clear light is thrown by this simple experiment on some clinical experiences. It is quite true that alkaline fermentation coincides in the great majority of cases with stagnation of the urine, and it is no less correct that the urine when undergoing alkaline fermentation always contains pus-corpuscles and epithelial cells, often in very large numbers; but the stagnation—to emphasise this point once more—never alone produces this decomposition of the urine, and it is also very exceptional for a purulent inflammation of the urinary passages to give rise to alkaline fermentation. When an abscess of the kidney or of its vicinity discharges into the renal pelvis or a submucous phlegmonous inflammation into the urinary bladder, the organisms entering with the pus may give rise to alkaline fermentation of the urine, just as they do to cystitis and pyelitis. Much more frequently, however, the converse relationship prevails, and *the decomposition of the urine precedes the inflammation.* Where an abnormal communication exists between the urinary passages and the vagina or intestine, &c., the exciter of fermentation may obtain admission from the latter parts; but the usual sequence of events is the conveyance, by means of an imperfectly cleansed *catheter*, of schizomycetes into the urinary bladder and urine, which till then was perfectly normal and had a normal reaction; and since the catheter will scarcely be employed except when the regular evacuation of the bladder has been prevented either by an actual obstacle or by muscular feebleness or again by loss of consciousness and sensibility, the organisms introduced meet, as a rule, with an all too favorable soil for their multiplication and development. Since Traube* first drew attention to this connection of events, genuinely *spontaneous* cases of alkaline fermentation of the urine, in which artificial introduction of the exciters of inflammation is excluded, have become some of the greatest rarities. This is true at least of the male: for the short and comparatively wide urethra of the female probably offers no insurmountable obstacle to the occasional passage of schizomycetes from the vagina and vulva into the urinary bladder. What far-reaching importance attaches to the artificial introduction of these organisms, in the production of alkaline fermentation, is nowhere more clearly taught than by the history of pyelitis and cystitis. It was with good reason that I just now stated how exceptional it is for these inflammations to become the cause of alkaline fermentation of the urine; for a very violent and even ulcerative inflammation of the pelvis of the kidney may be set up by calculi, and pronounced suppurative pyelitis may develop in the course of infective diseases—yet the urine, though it contains a copious sediment of pus-corpuscles and epithelium, always remains *acid* till some necessity, such as may readily arise in these cases more particularly, requires the use of the catheter or sound. Should the instrument be dirty, the urine which has for weeks preserved its acid reaction despite the calculi and pyelitis, may become alkaline within twenty-four to forty-eight hours.

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* Traube, 'Ges Abhandl.,' ii. p. 664; 'Symptome d. Krankheiten d. Respirations- und Circulations-Apparats,' p. 117.

While we have here what I might almost call an accidental conjunction of inflammation of the mucous membrane and fermentation of the urine, in which a dependence of the latter on the cystitis or pyelitis is altogether out of the question, those cases in which the inflammation follows the decomposition of the urine are, as already noticed, very much more frequent. It is indeed open to discussion whether the decomposing urine or the quantities of bacteria contained in it set up the inflammation of the urinary passages, and the latter alternative may be supported by the circumstance that, in the kidney itself, the colonies of micrococci which have penetrated into the urinary tubules are surrounded by foci of purulent inflammation; at any rate the fact remains that after the urine has become alkaline, the mucous membrane in contact with it very soon undergoes a severe hæmorrhagic purulent inflammation. Not only so, but the inflammation is very frequently complicated by a more or less deep *necrosis*, so that the process acquires a marked *diphtheritic* character. As for this necrosis also, it has not yet been made out whether it should be attributed to the action of bacteria—in the pyelonephritic foci, the suppuration is mostly preceded, you are aware, by a local necrosis—or whether it is referable to the corrosive action of the ammoniacal urine. One undoubted effect, however, of the carbonate of ammonia contained in the urine is the *mucous and gelatinous appearance of the thick sediment* thrown down in these cases. Nothing would be more erroneous than to speak of a *catarrh of the bladder* on the strength of the mucous consistence sometimes characteristic of the whole amount of urine. Whether an actual catarrh ever occurs in the bladder, *i. e.* an inflammation of the mucosa accompanied by an abundant production of mucus, may perhaps be questioned, as has been done by Traube.* The mucoid masses in our alkaline urine certainly do not consist of mucin, but of albumen, and are nothing but the products of the action of the carbonate of ammonia upon the pus-corpuscles and epithelial cells contained in the urine; precisely the same muco-gelatinous consistence is produced in a purulent fluid on adding ammonium carbonate or caustic ammonia in a test-tube. Moreover, the secondary processes observed to occur during alkaline fermentation in urine preserved in the air without any special protective measures, also set in in the urinary passages when the same decomposition has taken place. Here too, oxalate and phosphate of lime are first precipitated; after the process has lasted for a time, large quantities of *crystalline ammoniaco-magnesian* phosphate separate out, and a deposit of amorphous urate of ammonia occurs. Now, if the surface of the mucous membrane is necrotic in places, the affected spots not only become deeply stained with urinary pigment but *encrusted* with precipitated salts; and in this way the mucous membrane of the bladder, ureter, pelvis of the kidney, and—in vesico-vaginal fistula—of the vagina as well, acquire an uneven and rough surface, often for considerable distances, so that to the examining finger the sensation is given of contact with a piece of emery-paper or even a file. Under these circumstances the urine is always extremely cloudy when passed, and throws down a copious precipitate, in which the pus-corpuscles and epithelial cells have for the most part lost their sharp contours under the influence of the carbonate of ammonia; the large quantities of crystals of triple phosphate appear characteristically prominent, and a great amount of amorphous organic and inorganic material is also invariably present. The sediment may be allowed to settle as completely as possible, and the clear urine above it may be repeatedly filtered, yet the cloudiness, far from being removed, will scarcely be reduced; for it mainly depends on the *micrococci* and other *schizomycetes* which are contained in every drop of the urine, sometimes in enormous multitudes.

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* Traube, 'Ges. Abhandl.,' iii, p. 11.

Among the changes undergone by the urine in the urinary passages, we must now devote a few words to the formation of *concretions*, to which reference has so often been made. The urine is naturally very specially predisposed to deposit concretions, because it not only abounds in saline matters but contains several salts which are very far from being easily soluble; I may remind you of the urates, the oxalates, and—when the reaction is only slightly acid—the earthy phosphates also. It is for this reason, as you know, that the urine, more especially if concentrated, deposits when cooled a reddish precipitate—the so-called *sedimentum lateritium*—which is redissolved on warming, and consists simply of urates less soluble in a cold than in a warm medium, more especially of urate of soda. Now change of temperature is not, it is true, a factor which can play a part in the separation of concretions within the urinary passages; and all thoughts too of a precipitation of the salts as the result of simple concentration of the urine in the urinary organs must here be more decidedly rejected even than in the case of the formation of biliary concretions. For we know nothing whatever of the occurrence of an absorption of water alone from the urinary passages, and while there is no doubt that all the substances present in the urinary concretions were previously constituents of the urine secreted by the kidneys, yet more or less profound chemical processes must take place, in order that these substances may be de-

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posited from their solution. Daily experience also teaches, however, that the urine forms a very favorable medium for the occurrence of such processes. Its acid reaction usually increases for the first few hours after being passed, and if the sediment be then examined, there are found, instead of urates or together with them, crystals of free *uric acid*, occasionally mixed with crystalline oxalate of lime. That no conclusion can be drawn as to the amount of urates contained in the urine, from the crystalline deposit of uric acid any more than from the sedimentum lateritium, has long been known, and has moreover been determined by Bartels* by numerous comparative quantitative analyses; it is simply the greater acidity of the urine that causes the uric acid to separate out from its alkaline combinations, and, since it is soluble with difficulty, to immediately crystallise. But the effects produced in the urine after it is passed by this so-called *acid fermentation* must also take place under certain circumstances within the urinary passages. For there are many persons whose urine contains crystals of uric acid even *at the time of its evacuation*. The separation of crystals is sometimes so slight as to result only in a faint cloudiness of the secretion; at other times their number is so great that the urine when passed throws down an abundant powdery sediment. The presence of these crystalline materials, usually termed *renal sand*, cannot easily be productive of mischief, since the granules are too fine to be arrested in any part of the urinary passages; but larger masses are very often formed in the pelvis of the kidney, some of which, capable of passing without much difficulty through the ureter, are called *renal gravel*, while the more bulky concretions are denominated *renal calculi*. The latter differ greatly in size; most commonly we meet with examples varying between the dimensions of a small pea and a bean, yet I only recently referred to the large coral-like branched calculi, which form actual casts of the pelvis and calices and almost completely fill up their cavity. But however striking the contrast may be, there are no real chemical differences between the renal sand, renal gravel, and renal calculi of this kind. For they consist solely of *uric acid*, mixed at most with a few urates.

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* Bartels, 'Deutsch. A. f. klin. Med.,' i, p. 13.

All these concretions are hard; they are also *coloured*, varying in shade from a red to a red-brown, or from greenish-brown to black-brown; as they increase in size their colour usually becomes deeper. In the smaller concretions, the fracture is mostly crystalline; in the larger stones it is usually stratified, and at the same time very dense, often strikingly reminding one of timber; the surface of the latter is generally smooth and even or slightly undulating, however irregular the general conformation may be. We are unfortunately very imperfectly acquainted with the conditions under which these smaller and larger concretions originate, despite the numberless chemical investigations which have been directed for a great many years to this point, and the many opportunities which present themselves for observing patients with renal concretions. An excessive production of uric acid is no more responsible in the great majority of these patients than it is for the production of the sedimentum lateritium. One thing is certain, however,—that uric acid concretions *can be deposited only in highly acid urine.* But if we are required to state on what the intensely acid reaction of the urine depends, our position becomes one of great perplexity. It was natural to turn first of all to the habits of the patients, particularly as regards diet; but the evidence brought forward for this connection is, if possible, still less trustworthy than is the similar evidence as regards the development of gout. Renal concretions occur with very varying frequency in different countries, yet each has its *fable convenue;* in one country new wine is accused, in another the excessive consumption of potatoes and other amylaceous foods which are supposed to give rise to lactic fermentation in the alimentary canal. Yet it is unnecessary to dwell on any of these assumptions, the more so as it is, as a rule, impossible to determine in individual cases whether the urine is thus acid when secreted by the kidneys, or whether it becomes so after secretion in consequence of a kind of acid fermentation, occurring in the interior of the urinary passages.

The increased acidity of the urine does not, however, explain the formation of the larger concretions, in particular of the uric acid stones. In fact, many persons who almost constantly pass more or less large quantities of renal sand, permanently escape the formation of true urinary calculi, while, on the other hand, large calculi may become established in the pelvis of the kidney without sand or gravel ever having been noticed in the urine; true, there is also a large number of persons in whose urinary passages concretions of all sizes form. As to the causes of the formation of the larger uric acid concretions and stones in the pelvis of the kidney, we are compelled to have recourse essentially to hypothesis. Assmuth[*] attributes it to a peculiar crystallization of the uric acid, which does not separate out in the ordinary form of rhombic tablets or short rhombic prisms, but of long columns terminating at each end in a sharp point; what determines the uric acid to crystallize in this way he leaves undecided, though he claims to have artificially produced these crystals by strongly acidulating the urine with phosphoric acid, or by adding acid phosphates. It is long since it was first pointed out, and with justice, that the presence of any kind of *foreign body* in the pelvis of the kidney must be highly favorable to the precipitation of uric acid or urates, and that such a body may consequently form the nucleus of a renal calculus, which, if it be not soon expelled, will continue growing through the addition of successive layers of uric acid. Thus Greisinger found in Egypt the eggs of *distoma* forming the kernel of renal stones, and similarly it has been assumed that the nucleus of the calculi so commonly occurring in children consists of the remains of the uric acid infarcts, these leading to further precipitation. Much less confidence can be placed in the idea that flakes of mucus in a pelvis affected with catarrh may form the kernel of a renal calculus more especially in old people. Still the nature of the body constituting the nucleus is probably of little importance. Whoever believes the presence of a firm or soft foreign body in the pelvis of the kidney to be a sufficient cause for the gradual development of a large uric acid concretion will not be surprised at the frequency of urinary calculi. For to say nothing of blood-clots, casts, and shreds of epithelium, you will remember that oil-drops, bacteria,[†] and other corpuscular elements circulating in the blood are excreted from the kidneys with the urine, and, of course, first enter the pelvis.

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[*] Assmuth, 'Deutsch. A. f. klin. Med.,' xx, p. 397.

[†] According to Krücke ('Ueber d. Structur u. Entstehung d. Uratsteine,' I.-D., Jena, 1879) the nucleus of the urate calculi actually consists, as a rule, of bacteria.

Next to uric acid, which supplies by far the largest contingent to the renal concretions, *oxalate of lime* is most frequently met with amongst them; as regards it, I have already told you that its crystals are not rarely found together with uric acid in the sediment of urine undergoing acid fermentation. Since the oxalic acid of human urine is probably only exceptionally derived from particular constituents of the food, and is usually a product of the decomposition of uric acid, its occurrence in conjunction with the latter is intelligible enough; and if you consider, moreover, the very slight solubility of the calcic salt, which is the only compound of oxalic acid occurring in the urine, it will not appear surprising that the envelope-like octahedra of oxalate of lime are so often precipitated from the urine together with uric acid and urates. Yet here too we are ignorant of the actual conditions under the influence of which certain individuals pass, at intervals or even continuously, so much oxalate of lime in the urine that one may speak of a genuine *oxaluria*, while in others the process goes on to the formation of large oxalic concretions in the pelvis of the kidney. These stones are exquisitely tuberculated on the surface, and are hence also named *mulberry calculi*, while the single tubercles are studded over with points and spines, with the result that the calculi are capable of violently irritating and injuring the mucous membrane of the urinary passages. They are the hardest of all stones, and are usually dark greyish-brown in colour, with a dense, often radiating star-like, but never laminated fracture. As bearing on the origin of the oxalic concretions, special interest attaches to the comparatively common stones which are composed of alternate layers of oxalate of lime and uric acid. Mulberry calculi also occur with a nucleus consisting of uric acid, and conversely a nucleus of oxalate of lime has often been found in uric acid stones: indeed, it may be doubted whether microscopic crystals of oxalate of lime do not much oftener form the centre of uric acid stones than is usually supposed.

Very much less common than the forms just discussed are the *cystin-* and *xanthin-concretions;* of their origin we hardly know anything except that they are thrown down from *acid* urine. We are better informed, on the other hand, as regards the concretions which form in slightly acid, neutral or alkaline urine. Here we have to deal essentially with *earthy phosphates,* and in particular with basic phosphate of lime and ammoniaco-magnesian phosphate. The great tendency of feebly acid urine to become clouded owing to a separation of phosphates is known to every one. On a former occasion (vol. ii, p. 647) I called attention to the fact that the calcareous deposits so often met with in Bowman's capsules, the epithelium of the convoluted tubes, and in the open collecting tubes of the pyramids, are determined by the deficient acidity of the secreted urine, which is unable to completely hold the earthy salts in solution; true, it is probable that necrosis of the epithelium or some similar change must also take place in order that the precipitated earthy phosphates may adhere to and encrust the parts in question. But concretions are found in the pelvis of the kidney also which consist of phosphate of lime or ammoniaco-magnesian phosphate, or of a mixture of both these substances. Concretions composed solely of these bodies are very rare, it is true; but the formation of a superficial lamina of earthy phosphates on uric acid or mulberry stones is proportionately frequent, *i. e.* the phosphates become deposited as a *secondary* stratum upon the primary calculi. The principal seat of phosphatic calculi, however, is the urinary bladder, and it is here at any rate that they attain their greatest dimensions.

That the various concretions can separate from the urine in the bladder just as in the pelvis of the kidney, provided the factors determining the separation are present, need not be mentioned expressly. Indeed, the circumstance that the urine regularly remains in the bladder at any rate for a much longer time than in the pelvis of the kidney must favour the deposition of sediments; and one might be inclined *a priori* to localise the place of origin of the urinary calculi in the bladder rather than in the pelvis of the kidney, were it not that the impaction of stones in the ureter has been certainly determined by clinical observation and the extreme frequency of renal calculi by pathologico-anatomical examination. As a rule, it will be difficult to make out whether the uric or oxalic nucleus of a vesical calculus has been formed in the bladder itself or has previously existed as a renal stone; nor does any far-reaching interest attach to this point. But it is possible to say positively that a stone has originated in the urinary bladder when its nucleus is formed by a foreign body which cannot ever have occupied the pelvis of the kidney, such as the broken point of a catheter introduced into the bladder or a silk thread which had slipped into it from a vesico-vaginal suture. Still such calculi are in a decided minority as compared with those whose nucleus is formed like that of the renal stones. Hence all that has been said of the latter applies also to the vesical calculi, except that these may become larger than the renal stones and that, as already stated, the earthy phosphates usually participate to a greater extent in their growth. This will happen more especially in the presence of hypertrophy of the prostate, stricture of the urethra, or some other cause which gives rise to stagnation of urine in the bladder. That the urinary stagnation should itself constitute a cause of stone, as held by many, is of course out of the question, while it cannot, on the other hand, be denied that the stagnation is decidedly favorable to their formation. Why the earthy phosphates participate so largely in the growth of the stones is also perfectly clear; the cause is simply the *alkalinity* of the urine which so commonly develops under these circumstances. It is not the presence of a stone or stones, nor is it the retention that renders the urine alkaline; but the calculi only too often give occasion for the use of the catheter or sound, while if the stone itself does not call for it, the retention of urine does, and thus the alkaline fermentation sooner or later sets in. From this time forwards phosphate of lime and then ammoniaco-magnesian phosphate are deposited, leading to the formation of the so-called *phosphatic calculi*, which are sometimes so voluminous, and which are strikingly distinguished from the uric acid and mulberry varieties by their grey to greyish-white colour and their comparative softness. Those more especially which consist chiefly of basic phosphate of lime are soft, their fracture earthy, and their surface smooth, as a rule; the more the ammoniaco-magnesian phosphate preponderates the more crystalline is the fracture, while the surface is then usually rendered uneven by pectinate or dendritic irregularities. But these concretions cannot even then give rise to such violent irritation, or wound the mucous membrane of the bladder so readily, as do more especially the mulberry stones ; and if, nevertheless, the phosphatic stones may occasion much greater suffering than the mulberry or uric acid concretions, this is due to the cystitis which, you are aware, develops at once under the influence of the alkaline fermentation of the urine. For the rest, if the urine was already alkaline when the stone-formation in the bladder began, the calculus may consist exclusively of phosphates ; on the other hand, should the physician succeed in removing the alkalinity of the urine, despite the presence of the concretion, uric acid and oxalate of lime may be thrown down upon the phosphatic stone, till the urine again becomes alkaline, when a white stratum of phosphates is again deposited upon the coloured layer.

Although we have repeatedly considered the act of *evacuation of the urine* in the foregoing discussion, it must now be further briefly dealt with, since some points connected with it have not as yet been referred to. That the urine does not at once leave the body when secreted is rendered possible solely by the existence of the receptacle formed by the urinary bladder ; hence when the bladder is absent, as in ectopia vesicæ, or even when abnormal openings are present in it, the evacuation of the urine ceases to be completely under the control of the individual. Of the abnormal openings, we have already discussed the *vesical fistulæ*, and as for the distressing malformation just mentioned, it not uncommonly affords us an opportunity of convincing ourselves of the strength of the peristaltic contractions of the ureters, by which the urine is sometimes during active secretion discharged in jets from the orifices of the ureters.

But even supposing the bladder to be normally present and that none but the physiological openings exist, its regular evacuation is not thereby guaranteed. The act of micturition is anything but a simple one ; reflex and voluntary contractions of the muscles combine in carrying it out, and the possibilities of derangements are many. If I may remind you briefly of the physiological process, it is the stimulation of the sensory nerves of the mucous membrane brought about by the gradual filling and stretching of the bladder that reflexly initiates the contraction of the detrusor muscle. The centre for this reflex has been incontrovertibly proved by Gianuzzi* and especially by Goltz† to lie in the lumbar region of the cord, the nerves engaged running principally in the bundles of the third, fourth, and fifth sacral. When the first few drops of urine enter the urethra, we become aware of the need for making water, which can be controlled for a time by voluntarily strengthening the contraction of the sphincter vesicæ, or can be yielded to, and the urine permitted to escape. In the latter case we can voluntarily assist the action of the detrusor by contraction of the abdominal muscles, and can reduce the only physiological resistances that oppose the efflux of the urine from the bladder by voluntary relaxation of the sphincters; for the elasticity of the prostate and of the tissues surrounding the urethra hardly constitutes an obstacle to the flow. It is not necessary, it is true, to resort to the aid of the abdominal muscles or to relax the sphincters in order to empty the viscus, as is most strikingly proved by Goltz's dog with the cord divided, which, in spite of the complete paralysis of the hinder part of the body, can pass a strong stream of urine and perfectly evacuate the bladder.

You all know how extremely unequal are the intervals at which different individuals micturate, not merely owing to the different quantities of urine produced, but because of the unequal capacity of the bladder, habit, &c. Some persons do not empty the viscus till it contains 500 to 600 c.c. urine or more, while others make water when the bladder is hardly half or even a third so full, without there being anything morbid in their different practices. We do not term the condition morbid till the periods at which the urine is passed deviate very noticeably from these physiological limits. The stimulation of the sensory nerves of the bladder is then the main determining factor. Usually, these nerves are excited, as has been said, by the stretching of the bladder-wall, and where the organ is capacious and free to expand a long time may pass before the stimulation is strong enough to initiate a contraction of the detrusor. But if, in consequence of a gravid uterus, a large ovarian tumour, a prolapse or other dislocation of the pelvic viscera, it is made impossible for the bladder to unfold itself and expand, the stimulation of the sensory vesical nerves will take place so much earlier that a contraction of the vesical musculature and therewith the need for micturition ensues even when the bladder is only slightly filled. This is, if possible, still more markedly the case in many pathological conditions of the interior of the bladder by which the sensory nerves are abnormally stimulated. Thus *the frequent desire to make water* is one of the most constant and troublesome symptoms of cystitis, of all ulcerative processes in the bladder, of most of the tumours occupying it, and is especially frequent in cases of vesical calculus. A nervous hyperæsthesia of the bladder also occurs, and may lead to an urgent necessity for making water, a complete *tenesmus ad matulam*, when the bladder is only very imperfectly filled. What renders all these cases the more painful is the very intense suffering which so commonly accompanies the contraction of the vesical musculature and discharge of the urine.

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* Gianuzzi, 'Rivista scientifica,' i, p. 41.

† Goltz, 'Pflüg. A.,' viii, p. 474.

So soon as the detrusor is caused to contract, the emptying of the bladder usually follows easily and rapidly, because the sphincters, even if not voluntarily relaxed, do not present any resistance that cannot readily be overcome by the detrusor. Yet the circumstances are not always so favorable. In the first place, there occur, and by no means infrequently, *tonic contractions of the muscles engaged in closing the bladder and urethra**—the latter only in the male—which though they usually pass off after a comparatively short time, may yet absolutely prevent the discharge of urine so long as they continue; a still commoner impediment, however, is produced by one of many *organic* conditions impeding the emptying of the bladder. I lately mentioned those most frequently met with; they are *vesical calculi* obstructing the *orificium internum urethræ*, *polypous tumours* in the region of the trigone, *tumours of the prostate* and *constrictions of the urethra.* The earliest effects of these impediments, more especially of the permanent kinds, are identical with those observed in all cavities surrounded by muscular walls—*dilatation* of the urinary bladder and *hypertrophy* of its *muscular coat.* Whether both these develop *pari passu*, or one preponderates over the other, probably depends essentially on the nutrition and strength of the individual affected, and, in the next place, on the degree of the impediment and especially the time occupied in its development. The more vigorous the individual and the less his general health is disturbed, and, further, the more slowly the narrowing has arisen, the more certainly may we expect an hypertrophy of the vesical musculature. The resulting condition is the so-called *vessie à colonnes*, in which the muscular bands project into the interior of the cavity like huge *trabeculæ carneæ*, while the wall of the contracted organ may measure as much as 2 cm. and more. Such a bladder is at the same time capable of enormous distension, which is perhaps facilitated by the formation in places having little muscular substance of smaller or larger saccular dilatations, so-called *diverticula.* But these diverticula are also found in bladders which are merely extremely dilated and in which the musculature is only slightly hypertrophied. Moreover, should the obstacle have arisen with absolute suddenness, as *e. g.* when a stone becomes impacted in the urethra itself, the wall of the enormously distended bladder may be reduced to the thinness of paper. Naturally, the dilatations accompanied by hypertrophy are much more favorable as regards the function of the bladder than are the simple dilatations. For although in the former a long time elapses between the single evacuations, and the act itself is extremely tedious, yet the affected individuals succeed in *completely emptying* the bladder, a thing which is hardly possible without artificial means in cases of pure dilatation. But there are much more serious disadvantages. For the less the bladder itself is capable of overcoming the hindrance—and its power to do this is directly porportional to the strength of its muscular wall—the more and the oftener is the use of the catheter indicated and the greater consequently the danger of cystitis and pyelitis. It was chiefly these cases I had in mind when I stated that urethral stricture and other obstacles to the emptying of the bladder, may prove injurious to the renal function even; for if the bladder is not in a position to overcome the impediment, the stagnation of urine must after a time be propagated to the ureters and pelves of the kidneys, with the result that finally all further flow from the kidneys ceases and the calamitous effects of complete anuria set in.

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* Cf. Esmarch, 'Langenbeck's Archiv,' xxiv, p. 589.

To produce *retention of urine*, however, it is not indispensable that abnormal resistances should oppose the evacuation of the bladder, since the same functional disturbance must also ensue when, the resistances remaining perfectly normal, *the contractile power of the detrusor is inadequate* and too feeble. That new growths of the bladder-wall or external adhesions should ever be attended by this result, is scarcely to be expected, for, just as in the case of the heart, the musculature of the bladder can gradually adapt itself to these impediments, so that while the evacuations are more frequent than natural, they are completely or almost completely effected. But a *feebleness* of the muscular wall going on to complete paralysis, may develop in the train of severe acute, and especially chronic, pyrexial diseases; and it has also been repeatedly noticed that persons who have for a long time voluntarily resisted the inclination to make water have afterwards been unable to empty the bladder, because the function of the detrusor had been temporarily destroyed on account of the excessive distension. Lastly, the extensive domain of *disturbances of innervation*, to which the detrusor extremely often falls a prey, have also to be considered here.

Everything that depresses the tone and contractile energy of the *sphincter vesicæ* must of course have precisely the opposite effect of detrusor-paralysis,—that is, the power of retaining the urine in the bladder is more or less completely lost, and *incontinentia urinæ* is the result. Owing to chronic inflammatory, ulcerative and cicatricial processes, the sphincter may be in great part destroyed, and the urethra, more especially in the female, may be converted into an actually rigid canal. Moreover, in consequence of artificial dilatation or of severe bruising during labour, the sphincter may become paralysed for a longer or shorter time. And, just as with other muscles, the sphincter is liable to paralysis from over-exertion, *i. e.* after unduly resisting the call to micturate. Finally, this muscle is extremely often the seat of disturbances of innervation, from its most slight degrees, as the enuresis nocturna of children and drunken persons, to severe and persistent paralysis.

In themselves these conditions appear very simple. If the detrusor is paralysed, the bladder cannot be emptied and *retentio urinæ* occurs; while if the sphincter is paralysed, the urine flows away against the will of the affected individual, at intervals and in quantities which depend on the completeness of the paralysis and the amount of elastic resistance of the prostate, &c. Again, if both the detrusor and sphincter are paralysed, as so often happens, *e. g.* after long resisting the call to micturate, and more especially in many diseases of the spinal cord, the result is a condition which is usually termed *ischuria paradoxa*, *i. e.* retention together with incontinence; the patient cannot regularly empty the over-filled bladder, while the urine trickles continually, as if from an overflowing vessel, through the urethra. At the sick-bed, however, the symptoms met with by the physician are by no means always so clear. In the first place, the patients do not always present themselves with a fully developed and complete paralysis, and if the affection of the spinal cord is still in its earliest stages, they suffer, not from retention, but from a certain *difficulty in making water;* the urine flows very slowly in a small stream, and they usually seek to aid its expulsion by contracting the abdominal muscles; or, there is not as yet any incontinence, yet the patients have not the sphincter so completely under control as in health, and must at once respond to the call to make water. Much more interest is excited, however, by the manifold modifications of these disturbances which are occasioned by the varying seat of the actual disease, according as we have to deal with an affection of the *peripheral nerves* or of the *reflex centre in the lumbar cord*, or, lastly, with a focus of disease *above* the lumbar portion, by which the connection between the latter and the brain is interrupted. A decision in individual cases may often then be attended by great difficulties; yet the principles that must guide one may be clearly defined.* If the reflex centre itself has ceased to act, or all the motor nerves which pass from the cord to the bladder have lost their functional power, the inevitable result is ischuria paradoxa. In paralysis of the sensory fibres passing from the bladder to the cord, the patients are not conscious of the need for making water, nor do spontaneous evacuations occur; the affected individuals can, however, voluntarily evacuate the bladder from time to time, by the action of the abdominal muscles, relaxation of the sphincter, and central excitation of the motor centre in the lumbar cord. In focal disease of the medulla above the lumbar region, the question is, whether the sensory or the motor or both tracts together are interrupted. In all these cases, there occur from time to time regular and energetic evacuations of the bladder, just as in Goltz's dogs with divided cord, in which complete retention of urine occurs only during the first few days after the operation, and is owing probably to the disturbance of the lumbar cord in consequence of the operation. When the sensory tracts are interrupted, the evacuations occur unnoticed by the patient, and without any antecedent feeling of need; in paralysis of the motor tracts, on the contrary, the feeling is present, but the impending evacuation cannot be prevented by contracting the sphincters; and if, lastly, the interruption is complete, the whole act is withdrawn not only from the knowledge but from the control of the patient.†

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* Cf. the handbooks of diseases of the spinal cord, and A. Erb, in Ziemssen's 'Hand.,' xi, 2, p. 146.

† On the subject of this chapter compare the well-known medical and surgical handbooks, *e.g.* Ebstein in Ziemssen's 'Handbuch,' König, Bardeleben, Pitha-Billroth, Hüter, &c.

CHAPTER VI.

CONSTITUTIONAL EFFECTS OF DISTURBANCES OF THE URINARY ORGANS.

Physiological office of the urinary apparatus.—Excretion of normal urinary constituents, poisons, and highly organised substances.—Sugar.—Fat.—Albuminuria.—Quantity of albumen lost.—Compensation by increased supply.—Hydræmia.—Its cause in renal disease.—Effect of oliguria on the water-contents of the blood.—Hydræmic plethora.—The dropsy of renal disease.—Bright's explanation of the dropsy by the hydræmia.—Bartel's theory of water-retention.—Localisation of the nephritic œdema.—Explanation of the nephritic anasarca as due to a diseased condition of the skin.—Explanation of the œdema of chronic nephritis by disturbance of compensation of the heart.—Characters of the renal hydrops.

Other morbid phenomena of renal disease.—Uræmia.—Its dependence on a diminution of the urinary excretion.—Experiments.—Accumulation of urinary constituents in the body.—Frerichs' ammonia-theory of uræmia.—Traube's theory of an œdema of the brain.—The uræmia is the result of the accumulation of urinary constituents in the blood.—The uræmic symptoms traced to their causes.—Acuteness and chronicity of the nervous symptoms.—Uræmic disturbances of the digestive process.—Hæmorrhages.—Retinitis albuminurica.—Tendency in persons suffering from renal disease to inflammations.—Uræmic œdema.

HAVING analysed and carefully considered, in the foregoing chapters, the nature and conditions of the various disturbances of function of the urinary apparatus, we have now to discuss *the effects of these disturbances upon the organism.*

You will not, I think, imagine that it is my intention to give an account of the symptomatology of the various diseases of the kidneys, bladder, &c. This we shall leave altogether to special pathology, which supplies full information as to whether one of the diseases in question is accompanied by pain; as to the condition of the kidney or bladder on physical examination; as to whether and when these affections are associated with pyrexia, and the like. All these form important and weighty points in the diagnosis and clinical estimation of the different diseases of these organs; but with the actual office of the urinary apparatus they have nothing to do. To this, morbid physiology must exclusively confine itself; it must be our business, therefore, to consider whether, and if so in what direction, any kind of functional disturbance prejudices the physiological office of the urinary organs, and we must further determine what influences are exerted by this possible prejudice upon the organism.

The office of the urinary apparatus is, you are aware, *the excretion of the non-gaseous waste products of the metabolism* from the body. The chief importance here attaches to the final products of the oxidation of proteids, which leave the body almost exclusively by the kidneys; in the next place, the *soluble salts* and the *water* are in greatest part removed by this means, so that the kidneys may be regarded as the most important regulators of the water-contents of the organism: lastly, some materials which have more or less accidentally entered the body are expelled from it with the urine. No other substances should normally be excreted through the urinary passages; and I desire in particular once more to expressly emphasise the fact that only the *final products* of the metabolism, but no kind of more highly organised materials, should be discharged in the urine. Now I have repeatedly called attention to the extreme variations which may normally occur in the quantities of urea, uric acid, water and salts excreted in twenty-four hours, nor have I concealed from you that mere figures are *per se* absolutely worthless. They only become valuable when compared with the nitrogenous matters, salts and water introduced into the individual's body during the same period; and if such a comparison be made, figures, which taken alone seemed surprising enough, are very often found to lie within the normal limits. Only when the excretion of the oft-mentioned substances considerably exceeds or falls short of the values which are usually found to prevail in healthy persons living on the same diet, are we obliged to have recourse to some kind of irregular process in the organism. But we may in the case of the urinary apparatus go a step further. We need not hesitate to declare that *the excretion of the normal urinary constituents,* however greatly increased, *can never involve a loss to the organism.* It is certainly not without significance that the urine in pyrexia contains more urea, in leukæmia more uric acid, than should be the case considering the diet of the patients in question; moreover, the abundance of urea contained in the urine of acute phosphorus poisoning, and its richness in lime in multiple caries of bone, are assuredly noteworthy indications of the occurrence of morbid processes in the body; *but the abnormally increased excretion of these substances is not the morbid factor.* These bodies are excreted in excessive quantities simply because they are present in excess in the juices of the body, and their removal from it, instead of being a loss to the organism, constitutes, as you will presently hear, a valuable service, since it is hardly possible that the body could have made use of the urea, uric acid, and salts. At most as regards the water, it might be questioned whether a very marked increase of the urine will not prove injurious to the organism by abnormally reducing its water-contents. This of course does not apply to the polyuria of the beer-drinker or of persons suffering from glycosuria; for it, you know, depends solely on the increased supply of water to the body. But the question is apparently justified in those cases of diabetes insipidus, with respect to which I attempted to establish a probability that they are due to active congestion of the kidneys (vol. iii, p. 1140), when the polyuria would consequently be *primary.* As a matter of fact, it has been thought that the frequency with which the diabetic are attacked by caseous pneumonia and other inflammations leading to caseation, should be connected with the great loss of water through the kidneys, and that the proximate cause of the caseation is the tendency, owing to the loss of water, of any chance inflammatory infiltrations and exudations to become dry and inspissated: an interpretation which, it is true, depends on an erroneous conception of the process of caseation. Not only, however, is the dependence of the caseous process on the polyuria untenable, but the loss of water is attended by no pathological results whatever, since the organism, warned by the sensation of thirst, always replaces the water withdrawn from the blood through the urine by a corresponding supply. Did the supply cease, or were a patient suffering from polyuria deprived of water, a certain degree of anhydræmia would certainly be the inevitable result. Yet we may reasonably doubt whether it would ever attain the same degree of severity as in cholera; for when the water-contents of the blood have fallen perceptibly below the normal, even a strong arterial congestion can hardly give rise to a profuse secretion of urine: the polyuria would in a sense put an end to itself.

But the excretion of *abnormal* urinary constituents is a different matter. Not that it always results in a loss to the organism! On the contrary, when foreign substances have accidentally entered the body, their removal is in every way desirable, especially if they are of a poisonous nature; and it also appears a most beneficial arrangement, even despite the resulting loss of highly organised substances, that the body can free itself in the urine of biliary constituents which have entered the blood and of hæmoglobin set free in it. An actual loss to the organism can accrue only through the excretion of substances which might be utilized for histogenetic purposes or for other activities and functions,—in particular, therefore, of substances which are usually included amongst the constituents of our food. In this respect it is of some interest that in various pathological processes, materials from the three chief categories of our food-stuffs are excreted in the urine; *sugar* in diabetes mellitus, *fat* in chyluria, and *albumen* in all varieties of albuminuria. Yet, though the excretion of any of these substances undoubtedly involves a loss to the organism, its significance cannot easily be accurately defined and estimated. In the case of sugar, the difficulty arises from our ignorance of the purpose to which it is applied, and of the manner in which it is used up by the organism. In one respect, on the other hand, this question is simplified by the fact that the abnormal loss cannot be made good by a corresponding abnormally large consumption of sugar or of such carbohydrates as are converted into sugar in the organism; for it is, as you will remember, a peculiarity of the diabetic patient that he is quite unable to assimilate sugar or cannot do so in sufficient quantities, so that an increased supply of carbohydrates is attended simply by an augmented excretion of sugar in the urine. To a certain extent the same thing occurs in chyluria; at any rate, it is expressly stated of some cases of chylous urine, that the quantity of fat was greatest some little time after a meal. Yet that any great importance attaches to this loss of fat is altogether out of the question. The quantity evacuated in the chylous urine never amounts to more than a few grams in the twenty-four hours,—a quantity, that is, which is quite insignificant when contrasted with the fat-supply. The fact that the chyluria can be borne for many years and decades without any impairment of the general health and nutrition shows clearly enough the absolute unimportance of these losses of fat, which, for the rest, owing to the great rarity of chyluria in Europe, can scarcely have any practical interest for us. That excited by albuminuria will be proportionately greater.

Few morbid symptoms have such a bad reputation and are so dreaded both by the public and by physicians as *albuminuria*, behind which constantly lurks, in the imagination of most, the bugbears of anæmia and hydræmia with dropsy and the other attendant consequences. It was long enough before even the unimportance of the transitory albuminuria occurring in fever and so many other conditions was recognised, and the necessity for considering the quantitative relations was perceived. For since albumen is not possessed of any peculiar mystical properties, it must obviously make a great difference whether the daily loss does not exceed one or two grams or whether the amount evacuated is ten times as great. We are not, it is true, so well acquainted as could be wished with the physiological history and significance of the albuminous substances of the blood-serum; still there can be no doubt that they, like other bodies, are incessantly used up in the metabolism of the organism and are no less incessantly replaced. If this be so, however, it is apparent that in judging of the consequences of albuminuria we must also take into consideration the albumen-supply; or, in other words, abnormal losses of albumen can only produce an impoverishment of the blood in this substance, when the body fails to make good the loss by increasing the supply. Women who nurse their infants lose very large quantities of albumen in the milk, day after day, for months together; and yet everyone knows that if they are healthy in other respects, and their diet is suitable and nutritious, so far from growing debilitated, they increase considerably in weight during the period of lactation and may acquire a roundness of form which they previously did not possess. Should you, however, raise as an objection—one inadmissible in principle—to the force of this illustration, that we have in this case to deal with a glandular secretion and not with a direct loss of albumen from the blood-serum, it must be admitted that it is no easy matter to adduce perfectly apposite examples from pathology, since the albuminous loss is then associated, as a rule, with other disturbances which more or less impair the general health of the patients. Thus, in dysentery absorption is invariably interfered with, while the inflammatory exudations into the serous cavities are always accompanied by pyrexia; on the other hand, in the apyrexial blènorrhœas of the urethra and vagina, the daily loss of albumen is much too slight to deserve attention as such. Large wounds, such, for example, as granulating amputation- or resection-wounds, may certainly be utilized for our purpose; it is nothing extraordinary for such wounds to produce every twenty-four hours for several weeks together as much as 120 to 150 c.c. of pus or even more, which involves—counting the albumen-contents of pus at 7 per cent. —a daily loss of eight to ten grams of dry albumen; and yet, in spite of these certainly not insignificant losses, the nutrition of such patients, if they are carefully tended, does not suffer in the least. But by far the most striking example is presented by the urinary apparatus itself. In chyluria, I just now stated, the general health of the affected individuals remains absolutely unprejudiced, although for years the urine contains, in addition to the fat, quantities of albumen amounting to from three to four pro mille and more, so that about six grams of albumen are daily withdrawn in this way from the body. Among the commoner renal diseases, also, there is one form which is very well adapted to deprive albuminuria of its character for danger; I mean the *contracted kidney*, where, though the percentage albumen-contents of the urine are wont to be very small, the loss of albumen during twenty-four hours is often as much as from six to eight grams, owing to the considerable increase in volume of the secretion. And yet every physician and pathological anatomist knows that persons with contracted kidneys can to the end maintain their strength and remain in an excellent state of nutrition despite the many years' duration of their illness.

But although it is accordingly unquestionable that the loss of large quantities of albumen can be fully compensated by a corresponding increase in the albumen-supply, it is not to be denied that, during the course of some renal diseases accompanied by albuminuria, the blood not uncommonly becomes markedly hydræmic. I told you, indeed, on a former occasion (vol. i, p. 452), that in hardly any other disease is the water of the blood so increased, and stated that a reduction of the albuminous contents of the blood-serum to almost half the normal, and a lowering of its specific gravity from about 1030 to 1016 or even 1013 have been repeatedly observed. Such extreme degrees of hydræmia are only imperfectly explained by the loss of albumen with the urine. It is certainly true that its albumen-contents, especially in amyloid nephritis, may sometimes amount to 4 per cent. or more; yet these cases are quite exceptional, and even then this enormous loss of albumen in the urine never persists long. In the very great majority of instances of chronic hæmorrhagic nephritis and even of waxy kidney, the albumen of the urine does not exceed 2 per cent., and often falls short of this, especially when the excretion is rather profuse. For in discussing this question, it is most important to bear in mind that when the urine is very rich in albumen *its volume is very considerably diminished*. If in twenty-four hours the total amount of urine containing 4 per cent. albumen be not more than 200 c.c., the absolute loss is not excessively great; and if—as should be done before forming an opinion as to the importance of the albuminuria—you calculate the daily values of the albuminous loss in cases of chronic nephritis, you may exceptionally meet with quantities of from 14 to 16 grams, but, as a rule, with not more than 8 to 10 or at most 12 grams *per diem.* But these values obviously do not differ so greatly from those above quoted as to render it impossible for the otherwise healthy organism to compensate the loss. Hence, it is a natural conclusion that the functional power of the body must in these cases be impaired in some other respect; or in other words, *that the albuminuria only leads to hydræmia when the organism is incapable of assimilating the amount of albumen necessary to cover both the physiological waste and the abnormal losses.* This supposition is, in truth, very strikingly applicable to the nephritic. For even those patients who are in a position to increase as much as they desire their albuminous food, are soon prevented by their disease from assimilating the albumen partaken of. You will presently hear that serious digestive disturbances regularly set in as the result of the retention of the urinary constituents in the organism, disturbances which of themselves would suffice to greatly impair nutrition. In patients suffering from the large waxy or butter-kidney, general nutrition is still further prejudiced by the effects of the amyloid degeneration, which involves the spleen, liver, intestines—in short, so many important organs; and it is, therefore, intelligible that precisely these patients should present the most extreme degrees of hydræmia.

Another factor has by many been regarded as an additional cause of the hydræmic condition of the blood in nephritis, namely, *the retention of water* in it. If it has been chiefly the clinician who has attached considerable significance to this relationship, he is no doubt supported by the fact that marked hydræmia always develops in the course of those renal inflammations in which the urinary secretion is essentially diminished. It is true that these are *per se* the most severe cases, in which, owing to the insufficient excretion of the urinary constituents, the setting in of digestive disturbances occurs earliest: still it is undeniable that the excretion of no other urinary constituent is so reduced as is the water of the urine. But however simple the entire connection between oliguria, water-retention and hydræmia may appear at first sight, the necessity of the connection is very far from having been actually proved. The believer in this doctrine neglects above all the manifold regulative capabilities of the organism. Were the quantity of water which is introduced into the body and produced by its metabolism in the twenty-four hours, constant; and were the amount of water excreted by the skin, lungs, intestine—in all ways, in fact, except by the kidneys—unchangeable; the effect of a reduction of volume of the urine on the water of the blood could be easily and definitely determined. But these are figures which are incessantly liable to the greatest variations. Thus, a very simple means of keeping the dilution of the blood within certain bounds, when the urinary excretion is reduced, is the restriction of the supply of fluids to the body. Just as a patient with diabetes insipidus or even with polyuria due to contracted kidney drinks copiously in order to make good the great loss of water, so a person from whose blood little water is withdrawn by the urinary secretion will take only small quantities of liquids, owing to the slight degree or absence of thirst. True, the quantity of water contained in our foods and produced by the metabolic processes is so great that complete compensation of extreme oliguria solely by abstaining from drinking is inconceivable. Here, however, the second means of relieving the blood of its superfluous water may be resorted to, namely increase of the extra-renal water-excretion. The loss by the skin is augmented even in persons with perfectly healthy and functionally capable kidneys, so that under certain circumstances, *e. g.* on vigorous muscular exertion or in a warm atmosphere, the water-excretion is many times greater than when the air is cold and the body at rest; and I need hardly call attention to the great difference in the loss of water from the intestines where the motions are hard and retarded as contrasted with profuse and frequent diarrhœa. But that these means are really resorted to by the organism where there is an excessive accumulation of water in the blood, we have already succeeded in establishing by means of experiment (vol. i, p. 459, *et seq.*). You remember that in dogs, in which we had produced a hydræmic plethora by the transfusion of large quantities of weak salt-solution, not only was the urinary, but all other secretions—saliva, gastric juice, succus entericus, bile and even pancreatic juice—increased, one earlier, another later, with varying degrees of profusion and without any definite order of succession, so that very profuse salivation sometimes preceded all excretion of urine, while at other times the bladder was repeatedly emptied during the experiment, before any saliva had flown from the jaws. No less clearly are we taught by the commonly occurring profuse diarrhœa of severe Bright's disease that the intestines play a much more important part in the excretion of water here than in health. But in order to be perfectly clear as to how the organism behaves in presence of a hydræmic plethora due to the retention of water, it is necessary above all to know how the excretion of water through the skin is influenced in these cases. Unfortunately, however, we have no certain means of forming an opinion on this point. Experiments on animals are here of little use, since it would be clearly improper to directly infer from the skin of the animals ordinarily experimented upon, with its thick covering of hair, to the skin of human beings; and as to the manner in which the excretion of water by the human skin reacts to a primary limitation of the renal secretion, there exist, so far as I know, no investigations that might serve our purpose. While all these circumstances greatly increase the difficulty of forming a certain opinion as to whether we have to deal in nephritis accompanied by oliguria, with only a simple, more or less severe, hydræmia, or with a hydræmia in which the blood-mass is at the same time increased, the question is rendered still more intricate by the very frequent occurrence in patients of this category of another complication which is eminently calculated to obscure the abode and exchange of the water.—I refer to *dropsy*.

How intimate is the relation between renal affections and dropsy is a fact so familiar even to the laity that it would be unnecessary to dwell on it here, even if we had not already done so in the chapter on hydræmia. That hydrops is one of the symptoms most commonly arising in the course of nephritis, all observers are unanimously agreed since Bright first recognised the connection: the nature of the relationship is the only point still admitting of discussion. Bright himself made the hydræmia the centre link in the chain; the albuminuria he regarded as the cause of this, and the dropsy as its consequence. Now, it is of course quite true, as we have ourselves recently stated, that considerable losses of albumen in the urine must gradually render the blood hydræmic, if not compensated by a correspondingly increased supply; and in evidence of this I have been able to quote figures, showing how extreme may be the degree of hydræmia in nephritis. But this is not enough to establish Bright's conclusion. For though it has been claimed that diluted blood will more readily transude through the capillaries than undiluted, this is nevertheless incorrect. On the contrary, I have repeatedly drawn your attention to the fact (vol. i, pp. 454, 519) that a very weak solution of albumen or extremely diluted blood may be conducted through the vessels of a rabbit's ear without any increase of the lymph-stream or a vestige of œdema, and you have yourselves been witnesses that a dog, in which almost half the blood-mass has been replaced by an equal or even greater volume of ·5 per cent. salt-solution, never displays even an indication of œdema. But should anyone consider that these results drawn from the dog and rabbit are not sufficiently convincing, I would ask him whether he has ever, in the absence of complications, observed in the subjects of exquisite hydræmia due either to repeated hæmorrhages or to sanguineo-purulent secretions and the like, such œdema as may in acute nephritis develop in the course of a few days? These cases of acute nephritis are invariably associated with a very considerable reduction in volume of the urine, and even if the albumen-contents amount to more than 2 per cent., the total absolute loss during the few days will at most be 20 to 24 grams—an amount not greater than that contained as serum-albumen in a pound of blood removed by venesection, to say nothing whatever of the blood-corpuscles. And such a loss of albumen which has almost no effect on a healthy man, and as the result of which certainly not a drop of fluid is poured out into the subcutaneous adipose tissue, is asserted to be sufficient to render a patient suffering from nephritis extremely hydræmic and to lead to the development of a general œdema!

Influenced by similar considerations, Bartels* more especially has endeavoured to substitute for the hydræmic theory another hypothesis, according to which the cause of the dropsy is *the retention of water in the blood.* Not the hydræmia *per se,* but only *the hydræmic plethora is asserted to give rise to the dropsy.* Unfortunately, however, the theoretic foundations of this hypothesis are still less securely established than are those of Bright's theory. As for the latter, the actual occurrence of hydræmia has been positively proved at least in a number of cases; but how little evidence there is for the existence of a hydræmic plethora in nephritis has just been thoroughly discussed. But even admitting that the blood-volume of persons, in whom the urinary secretion is abnormally scanty, is considerably in excess of the normal standard, is it conceivable that the organism, instead of resorting to the ordinary channels for the excretion of water, should utilize the skin and subcutaneous tissue as a water-reservoir? That this does not happen in the dog and our other mammalian domestic animals, and in particular that it does not occur in those species which are furnished with actively functional sweat-glands, you know from the experiment on hydræmic plethora. For we could venture on allowing enormous quantities of ·5 per cent. salt-solution to run into the vascular system of the animal without even an indication of anasarca setting in: that the previous ligature of the renal arteries makes no difference in the result is at bottom self-evident, and has, moreover, been determined by Lichtheim and myself by an experiment expressly directed to this end.† And what are the proofs on which Bartels relies in support of his view in man? In the first place, he dwells on the fact that only those renal diseases which are accompanied by oliguria certainly lead to dropsy: a fact which may be admitted, but which, as shown in our foregoing remarks, may be taken advantage of with at least equal justice by the adherents of the hydræmic theory. Bartels' chief argument is, that the increase and disappearance of the œdema are precisely in inverse proportion to the degree of diuresis. To establish this rule, Bartels has taken an astonishing amount of trouble:

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* Bartels, in Ziemssen's 'Handb.,' ix, 1, p. 89, *et seq.*

† Cohnheim and Lichtheim, 'Virch. A.,' lxix, p. 106.

for months together he has, in a large number of renal cases, compared the water-supply, the volume of the urine, and the dropsy, and has accurately recorded their relations, with the result that he has presented us with a series of figures which at first sight appear sufficiently striking.* And yet what do these arduous investigations really teach? Nothing except that increase of the dropsy, decrease of the volume of the urine, and increase of the quotient obtained by dividing the water-supply by the water-excretion always coincide, and that the same is true of decrease of the dropsy, increase of the urinary secretion, and decrease of the quotient. But—even if we overlook the fact that other observers have not infrequently failed to find such a regular relation between the dropsy and the volume of the urine—does it actually follow that the variations in the quantity of urine are the determining factor? So little is this the case that we might equally reasonably adopt the opposite conclusion, and infer that the increase and disappearance of the dropsy is really the essential element in the process: if the dropsy increases, the urine will *cæteris paribus* necessarily decrease, and if the dropsy disappears, *i. e.* becomes absorbed, the urine will no less inevitably increase. Not merely has Bartels failed to establish the likelihood of the dependence of the hydrops on the retention of water in the blood, but there are a number of pathological facts which directly disprove this view. I do not wish to remind you that a dog can survive the ligature of both ureters for almost a week, and yet never shows a trace of dropsy, despite an adequate supply of liquids. In man, too, Bartels himself brings forward a case, also referred to by me (vol. iii, p. 1230), where complete anuria lasted more than five days as the result of occlusion of the ureters, but was not followed by œdema; and a still more striking case has recently been communicated by Schwengers,† that of a patient aged 59, who suffered from complete anuria of nine days' duration, as the result of closure of the right ureter by a stone while the left kidney was absent, but without a trace of œdema or of effusion into a cavity up to death. Moreover, I have already informed you (vol. i, p. 454) that in hysterical cases anuria or at least extreme oliguria of still longer duration has been observed in the absence of dropsy. But while no vestige of hydrops occurs, the importance of these examples as regards the question now engaging our attention is not lessened by the fact that the patients suffering from anuria or oliguria repeatedly get rid of large quantities of fluids, more especially drinks, *per os* or *per anum*. For vomiting is also present in acute nephritis, and even were it absent, we should still have to explain why it is that the organism deposits the retained water in a region which it never at other times uses for the removal of water from the blood. How little the combination of hydræmia and oliguria suffices to produce such œdemas as occur in the nephritic is best shown, however, by the cases of unhappy women with carcinoma uteri, in whom, owing to the extension of the new growth or secondary implication of the lymphatic glands, both ureters become gradually occluded. The inadequacy of the urinary secretion is proved by the development in these cases of the complex of symptoms known as *chronic uræmia*, which will presently be more fully described; by this life is ultimately destroyed, and yet—provided there be no complication by thrombosis or other lesion of the circulation—one never sees more than a slight œdema of the ankles which may extend a little up the leg, while the enormous and wide-spread anasarca so characteristic of nephritis is altogether absent.

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* Bartels, loc. cit., p. 92.

† Schwengers, 'Berl. klin. Wochenschr.,' 1881, No. 34.

And here we meet with a highly important point, which is completely neglected both by the hydræmic and by the retention theory, namely *the localisation of the nephritic œdema*. Were the wateriness of the blood or were the overloading of the vascular system with liquor sanguinis the cause of the dropsy, might we not expect that the fluid would transude or be excreted into every part affording room for its accommodation, or at least into all the regions which are the chief seats of the dropsy in general disturbances of the circulation? Yet this expectation is not realised. Rather it is the rule that hydrops renalis is greatly predisposed to attack the *subcutaneous cellular tissue*. The dropsy of renal disease almost always begins as anasarca, and a considerable time may elapse before one of the serous cavities participates in it; these vities in many instances, indeed, escape altogether. It is not simply in the milder cases that the dropsy remains confined to the skin, but precisely in the most severe ones; where the nephritis has proved fatal in a short time the cavities may be quite free from fluid, while the anasarca has attained enormous proportions and involved the entire surface of the body. Moreover, as regards chronic nephritis, if we leave out of account those cases which are complicated by valvular disease or by pulmonary or hepatic affections, we find that in a number of instances the anasarca is the only manifestation of dropsy occurring during the whole of life. Nevertheless in chronic renal disease the predominance of the subcutaneous dropsy does not usually obtain to the same extent. Thus, in uncomplicated chronic Bright's disease, effusions into the serous cavities sooner or later make their appearance as well, and I have even observed, in the bodies of persons who had died of chronic nephritis, a hydrothorax or hydropericardium or other effusion into a cavity much more marked than the anasarca. With respect to the so-called waxy or butter-kidney also, my experience goes to show that the dropsy is here usually general, and attacks the subcutaneous cellular tissue as well as the serous cavities, though the affection of the latter is usually less marked; certainly the hydrops is more considerable in these cases than we usually find it in the bodies of persons who have died of cancer or in whom hydræmia has been produced by some other cause.

These experiences as to the wider distribution of the œdema in chronic renal inflammations does not, of course, alter the fact that anasarca is the only form of dropsy likely to be observed in fresh acute nephritis; and because a few days are here sufficient for the entire skin from the face to the feet to become œdematous and sometimes enormously so, it is natural to suppose that there would be no difficulty in discovering the internal conditions, on which this localisation of the dropsy in acute nephritis depends. But have we really here to deal with a direct relationship of dependence? Were this the case, every acute nephritis of some intensity must undoubtedly lead to anasarca. *This is not so, however.* It almost appears to me that so impressed have observers been by the rapid development of extreme anasarca in many primary and secondary renal inflammations, as, for example, scarlatinal nephritis, that too little attention has been paid to those cases of the same disease in which this striking symptom, supposed to be so characteristic, is absent. For such cases are by no means rare. I myself can recall more particularly the occurrence, during different epidemics of relapsing fever, of cases of acute nephritis due to the fever, which were accompanied by the absolutely pathognomonic functional disturbances of the kidneys—scantiness of the urine, marked albuminuria, copious sediment of colourless and red blood-corpuscles and casts—and which moreover, as I succeeded in many instances in discovering at the autopsy, were typical examples of acute hæmorrhagic inflammation; I can recall, I say, most vividly that in these cases, although the disease had lasted for weeks, there was either a *complete absence of subcutaneous œdema* or such an insignificant degree of it as is occasionally found in all pyrexial diseases when occurring in debilitated persons. Moreover, in nephritis after diphtheria of the pharynx and also after pneumonia, I have often completely failed to find anarsarca, although here too the symptoms of renal inflammation had been observed for weeks and its presence more than sufficiently demonstrated at the autopsy. Accordingly, it is evident that the nephritis with the functional disturbances directly occasioned by it, or at any rate the nephritis alone, cannot be the cause of the subcutaneous dropsy; some additional factor must concur in producing it. The nature of this factor has been already indicated when discussing the subject of hydræmia. So far as I see at least, it can be nothing but an *inflammatory alteration of the skin* or of the *cutaneous vessels*, in consequence of which these vessels are rendered *abnormally permeable* to the water of the blood. The inflammatory alteration of the vessels of the skin must either have preceded the nephritis or the noxa exciting the inflammation have simultaneously attacked the skin and the kidneys; the former alternative is certainly applicable to scarlet fever, the latter probably to the cases of so-called primary nephritis which are caused by the chilling or wetting of the skin. In scarlet fever, the inflammatory skin-affection at once gives evidence of its presence, and the inflammation is known to be sometimes so intense that complete anasarca sets in *without, or at any rate before, the development of nephritis.* On the other hand, an affection of the skin of such violence is very exceptional as the result of changes of temperature, moisture or the like: for the skin does not react to cold with redness or other perceptible symptoms, and does not usually become œdematous till the blood has açquired a certain hydræmic quality. Yet you will no doubt remember the cases of *acute dropsy of the skin after evident chilling*, to which attention was formerly directed (vol. i, p. 518); shall we really be too venturesome if we class this *hydrops irritativus* with the *hydrops scarlatinosus sine nephritide?* I do not fail to perceive, it is true, the various objections to our regarding hydrops irritativus as an inflammatory œdema. The fact of our unacquaintance with the agent exciting the inflammation applies not only to this but to many other processes of an inflammatory nature; yet we do not usually admit the occurrence of an inflammation without heat and without redness in parts so superficially situated. It is far from being made out, however, that the cutis itself is primarily affected and not rather the vessels of the subcutaneous cellular tissue, perhaps through the agency of the sweat-glands: and however this may be, one cardinal feature of genuine inflammation is certainly, under these circumstances, displayed by the vessels of the skin or subcutaneous tissue, namely the abnormally increased permeability. And this precisely is the essential element so far as our argument is concerned. In the higher degrees of the alteration in question, œdema is at once developed, as is usual in true inflammation; in its slighter degrees, on the contrary, the change is not sufficiently intense to augment the transudation to the extent of actual œdema. The case is, however, altered, as you know, when the blood is hydræmic, and especially when a hydræmic plethora sets in; for although little effect is exerted by the latter on the healthy extremity of a dog, we observed a very considerable increase in the flow of lymph from the inflamed leg, after some litres of salt-solution had been introduced into the vascular system of the animal. These experiences, in my opinion, afford a natural explanation of the anasarca of acute nephritis. In a person whose cutaneous and subcutaneous vessels are intact, these parts are not utilized to relieve the blood of any superfluous water it may happen to contain; but when the vessels just mentioned are abnormally permeable, the subcutaneous cellular tissue is used as a reservoir for the water which fails to be excreted in normal fashion by the kidneys. If this entire interpretation be correct, it is easy to see why it happens that the anasarca which forms so prominent a symptom in many cases of nephritis is altogether absent in others of equal intensity and duration. The anasarca depends on the abnormal permeability of the cutaneous and subcutaneous vessels; hence it will hardly be absent in all those cases where the primary or secondary nephritis has its starting-point in injury of the skin, while in relapsing fever and diphtheria—in short, whenever the skin is not directly implicated in the morbid process—the inflammation of the kidney, though associated with an equal degree of water retention, is absolutely unattended by the characteristic acute anasarca. Our theory, moreover, affords an explanation of the restriction of the dropsy in acute nephritis to the skin and subcutaneous tissue, while the serous cavities remain free.

When, moreover, during the course of chronic Bright's disease, the anasarca permanently forms a main feature in the case, we are also justified in assuming that the disease has had its starting-point in the skin, or that the skin and kidneys were together implicated from the first. This is true chiefly of the subchronic form, or to use Weigert's term, the chronic hæmorrhagic nephritis, whether setting in acutely or throughout insidious in its development and course. To decide on the nature of the hypothetical skin-affection is a matter of difficulty, more especially in the much commoner cases of the second category, simply because the commencement of the disease generally escapes detection. It has repeatedly been stated by writers that the skin in these patients does not behave quite normally: yet it is questionable whether the often-observed incapacity to sweat spontaneously is actually a sign of primary disease of the skin and not rather a simple result of the œdema, and of the anæmia of the skin set up by it. To me it appears most probable with regard to these cases also, that the special alteration consists in an abnormal increase of permeability of the cutaneous and subcutaneous vessels; is it not precisely these forms of chronic nephritis that have been referred by all writers to repeated chilling and wetting of the skin as their essential cause? But however adequate this hypothesis may be to explain the anasarca of these patients, which though liable to considerable variations as regards localisation and intensity, is yet as a rule persistent; it does not throw light on the dropsy of cavities, which, as already stated, only rarely fails to set in when the Bright's disease has lasted for a considerable time. It is still less applicable to the markedly chronic form of nephritis leading to contraction, where it is nothing unusual for anasarca to be completely absent for many years; and if during a temporary or lasting exacerbation dropsy sets in, the serous cavities are generally no less involved than the subcutaneous cellular tissue, the dropsical infiltration of which is often limited to the lower extremities, and certainly never forms so prominent a symptom in the chronic as in the subchronic, and more especially the acute, forms of nephritis.

These dropsies more especially are regarded by Bartels as strongly supporting the view maintained by him, according to which the hydrops is merely the reaction of the organism to the decrease in volume of the urine. Nowhere has he been more uniformly struck than in these chronic forms by the connection between increase or even setting in of dropsy and marked diminution of the urinary secretion, and similarly between the gradual disappearance of the dropsy and the increased secretion of urine. Yet he makes not the slightest attempt to explain why it is that in these chronic cases the serous cavities are no less liable to dropsy than the subcutaneous cellular tissue, while in the acute form the latter alone is chosen. You are acquainted with our reasons for rejecting the theory of water-retention; yet I have already remarked that for these dropsies the view enunciated by us of the anasarca of acute nephritis does not avail—especially in cases of contracted kidney which may go on for years without a trace of subcutaneous œdema, probably because they do not originate in damage to the skin. The key to the explanation of these dropsies is afforded by the absolutely correct observation which establishes the coincidence of their development with the decrease of the urine, though not, it is true, in Bartels' sense. When, during the course of a chronic uncomplicated nephritis, the usually abundant or even abnormally excessive secretion of urine is suddenly considerably reduced, to what is this change due? To nothing but *a disturbance of that compensation* of the renal affection *which was effected by the hypertrophy of the heart.* Whether this disturbance is caused by a pathological process which makes new and increased demands on the heart, or, as so frequently happens, by exhaustion of the hypertrophied heart-muscle, there must at once be a reduction of the urinary secretion, which is only maintained at such a considerable value by the high arterial tension: when the urinary secretion in these patients decreases, the small easily compressible pulse at once witnesses to the fact that compensation is disturbed. The cardiac hypertrophy of the nephritic depends on essentially the same conditions and has the same significance as the hypertrophy arising in various other vascular lesions: that which in one case is brought about by stenosis of the aortic orifice, in another by arterio-sclerosis, is here due to the obstruction of the blood-stream through the kidneys. It may be unreservedly said, indeed, that we have here a cardiac, or better a circulatory, lesion, which is distinguished in no respect from analogous lesions except by its local cause. If this be so, the further history of the nephritic cardiac hypertrophies must resemble that of the other forms; in other words, so long as the heart can meet the demands upon it, the entire circulation continues regular, but so soon as from any cause the functional power of the heart is reduced, the well-known consequences of the uncompensated cardiac lesions make their appearance. I recently mentioned (vol. iii, p. 1196) that inflammation of the kidney is no less capable than disease of the aortic orifice of giving rise to hypertrophy not merely of the left, but also of the right ventricle; I can now supplement this by saying that when compensation is seriously disturbed nephritic patients must develop the same œdema as do persons with so-called cardiac or circulatory lesions, in the narrow sense of the term. You observe that the œdema and oliguria are in chronic nephritis intimately connected; yet one is not the cause of the other, but *both are co-effects of the same cause, i. e. of the disturbance of compensation.* In other words, the œdema of chronic nephritis, except when inflammatory alterations of the skin are involved in its production, is an *œdema due to mechanical hyperæmia.* With this view it harmonizes perfectly that these dropsies implicate both the serous cavities and the subcutaneous cellular tissue, and indeed the resemblance to the dropsy of heart disease extends so far as to occasion precisely the same irregularities in the distribution of the hydrops of both categories in the various regions of the body. Everyone who has examined many heart cases *intra vitam* or *post mortem* knows that at one time ascites, at another hydrothorax, at a third anasarca preponderates, without our being able to say usually to what this varying behaviour is due; and precisely the same observations are made in individuals with chronic Bright's disease. Moreover, our interpretation makes the comparative frequency of *pulmonary œdema* in these diseases easily intelligible. The œdema of the lung has also been frequently classed with the other œdemas of renal disease and has been schematically regarded as a not altogether rare localisation of renal dropsy. With little justice, it is true! For you know that general pulmonary œdema is called forth by a sudden impediment to the efflux of venous blood from the lungs which cannot be overcome by the right heart, and is produced in the most striking way by *paralysis of the left ventricle.* And just as the remaining cardiac lesions by which increased demands are made on the work of the left ventricle involve a marked tendency to acute pulmonary œdema, so also in chronic nephritis with left cardiac hypertrophy; the mechanism of the œdema is here too the ordinary one, and it is only because the left ventricle of nephritic patients has constantly an abnormally large amount of work to accomplish that the danger of a more or less sudden paralysis is more menacing in them than in healthy individuals.

You now perceive why it is that in acute nephritis, as a rule, effusion into the serous cavities is not associated with the anasarca or is quite overshadowed by it. For if the dropsy of the cavities depends on general mechanical hyperæmia, it cannot well develop till the influence of the nephritis has told upon the circulation generally, and for this a certain period is under all circumstances required. It is not the nature or cause of the acute nephritis that is here the determining element, but solely its *acuteness;* the former affords an explanation only of how it happens that in numbers of cases the anasarca sets in early and with great intensity in spite of the acuteness. But you will not fall into the error of supposing that because this is so, patients with acute nephritis are exempted from dropsy of cavities. For if you consider that, as already stated (vol. iii, p. 1182), a severe nephritis is followed after a few weeks by the unmistakable signs of an increase of arterial tension, and that, more especially in children, a marked hypertrophy of the heart may develop in a short time as the result of acute scarlatinal nephritis, you will certainly, on the strength of these facts, come to the conclusion that an equally short time will under certain circumstances suffice to bring about a mechanical dropsy in addition to the anasarca already present. Just as you feel no surprise when in cases ending fatally, the dilatation often exceeds the hypertrophy of the heart, it will appear only too intelligible that a certain quantity of fluid should then be met with in one or other of the cavities.

We may further conclude from what has been stated that in cases of chronic nephritis in which from any cause cardiac hypertrophy fails to take place—hence in particular the *amyloid* form—some features of the uncompensated cardiac lesions will set in early, and amongst them the multiple œdemas. The fact that amyloid degeneration is extremely often combined with dropsy attracted the notice of pathologists very soon after the disease was first recognised. Its cause was sought in the hydræmia almost inseparable from amyloid disease, and a welcome confirmation of this view was supposed to be afforded by the fact that the œdema does not become really marked, as a rule, till the degeneration extends to the kidneys, when to the other disturbances is added the direct loss of albumen from the blood. This latter factor has, it is true, lost much of its significance since it was finally settled that the kidneys are always implicated in cases of amyloid disease of some duration. And we now know, on the contrary, that in very many of the cases of amyloid disease which run their course without any or with insignificant œdema the renal vessels are very extensively involved in the degeneration; and not merely when albuminuria is absent does this occur, but also when the urine secreted by amyloid kidneys contains, as it usually does, albumen, dropsy may nevertheless long remain absent. I have myself seen such cases, and there is no dearth of examples in the literature which show in a very evident way that the organism does not necessarily respond even to very considerable losses of albumen by dropsy—for I would remind you that the pure amyloid kidneys excrete a profusion of urine. As a general rule, it is true, œdema does occur in these cases: still in pure uncomplicated amyloid disease of the renal vessels, even when associated with degeneration of the spleen and liver, we scarcely find more than a moderate anasarca of the lower extremities with slight dropsy of some one or other of the cavities, such as are also observed in so many chronic diseases attended by a deterioration in the composition of the blood: when, on the other hand, you meet in amyloid degeneration with such extreme degrees of dropsy as are characteristic of acute and also of chronic nephritis, you may certainly count upon the presence, not of simple degeneration of the vessels, but of *true amyloid nephritis*. It is peculiarly the waxy or butter-kidney that is wont invariably to be accompanied by considerable and obstinate dropsy, that is, not only by anasarca but by effusions into some of the cavities. This does not depend upon any peculiar distribution of the amyloid process; rather I would emphatically state that the vessels of the subcutaneous tissues and cavities happening to be dropsical are only extremely exceptionally involved in the lardaceous degeneration. The amyloid change is but an indirect cause of the dropsy, in that it prevents the development of cardiac hypertrophy, and consequently early allows those effects of the circulatory lesion to set in which usually only arise on a disturbance of compensation. These are also *œdemas due to mechanical hyperæmia*, and though they often enough exceed in bulk the ordinary hydrops of cardiac disease, this is simply because the transudation in these very cases is derived from such extremely hydræmic blood. This hydræmia is also the cause of the unusual *poverty in albumen* of the dropsical fluids of patients suffering from renal disease. There is still a want of adequate researches dealing with the different etiology of the renal dropsies, yet all the statements in our possession agree in this, that *the dropsical fluid is an extremely watery one.* The known disparity in the albumen-contents of the serous fluids of the different localities is maintained in the dropsies of renal patients, but the fluids are everywhere poorer in albumen than are those of the particular regions at other times, so much so that the fluid of anarsarca sometimes contains only a few parts albumen *pro mille.* Formed elements are also only sparingly present in renal œdemas. Now, you perceive from all this that the dropsies occurring in disease of the kidneys are certainly not so like in their origin as to admit of our referring them, as has generally been attempted, to a single causal factor in all cases. I am very far from denying the occurrence of true *hydræmic* œdema in chronic nephritis; yet this form has never that intensity and wide distribution which we are taught to regard as distinctive of renal dropsy. Further, we may attribute to the *hydræmic plethora* a considerable indirect influence especially on the amount and constitution of the dropsy, yet we must decline to recognise in it an immediate and direct cause of the hydrops. Rather, I believe I have proved with regard to the œdema which has long been looked upon as specifically renal, namely the *anasarca,* that in acute nephritis it is always, and in the chronic forms frequently, conditioned, not by hydræmic plethora, but by certain alterations of the cutaneous and subcutaneous vessels closely allied to inflammation, which either precede the nephritis or are developed simultaneously with it. In the second place, we were able to refer a great part of the œdemas setting in during the course of chronic nephritis to the peculiar position of the renal vessels, or rather of the renal bloodstream, in the aortic circulation, a position by virtue of which disturbances of the renal circulation influence the general circulation in a different and much more serious manner than we know to be case in connection with any other organ. It is possible, meanwhile, that even yet we have not exhausted the etiology of the nephritic œdemas, and that a factor of a very different kind plays a part in their production, namely the retention—not of the water, but of the *solid urinary constituents* in the organism. This highly important point in the pathology of the urinary apparatus, which hitherto has only been touched upon superficially, must now receive more attentive consideration.

In addition to the disturbances of the urinary secretion and circulatory apparatus, as well as the œdemas just discussed, the course of the various renal diseases is marked by the occurrence of a number of other morbid symptoms, which, though not invariably present, are yet so frequent that Bright himself recognised their direct connection with the renal affection. These disturbances vary much in nature and importance: all the systems of the body may be affected by them; and since, moreover, they appear with very different degrees of severity, you must not suppose that the diverse forms of nephritis will present a uniform series of symptoms. Among the most common and earliest occurring, are various digestive disturbances. The nephritic very frequently complain of all kinds of *dyspeptic* troubles; they very often suffer from obstinately recurring *vomiting*, and though *diarrhœa* is less frequent, it is sometimes present in very violent form during the whole course of the disease, and may defy all treatment. The *skin* in nephritis is usually conspicuously pale, and at the same time dry and inflexible; a very tormenting affection in some cases is an occasionally insufferable *cutaneous pruritus*. Various disturbances are observed of the respiratory apparatus, usually paroxysmal in character, from short transitory dyspnœa to most typical *asthmatic* attacks. In many cases, a marked *hæmorrhagic diathesis* develops, which shows itself more especially as a tendency to bleeding from the nose, but also, though more rarely, in the occurrence of hæmorrhage from the stomach and intestines; moreover, *cerebral hæmorrhages* are not uncommon during the course of nephritis, and are occasionally so severe as to prove fatal; lastly, small bleedings form an integral part of so-called Bright's *retinitis*, also known as *retinitis albuminurica*, by which the vision of so many patients is essentially impaired. But besides this affection, there occurs another form of severe disturbance of sight, which is not dependent on palpable pathologico-anatomical alterations of the retina, and is strikingly distinguished from retinitis by its sudden origin and, perhaps, no less sudden disappearance; I refer to what is commonly termed *amaurosis uræmica*. Furthermore, the frequency with which persons suffering from renal disease are attacked by inflammatory processes has for ages attracted the notice of all observers; not only do we find erysipelas and phlegmonous inflammations, which might be connected with the anasarca, or diphtheritic inflammations of the intestinal tract, which, as you will soon hear, may be explained without difficulty, but the lungs, the bronchi, and the region of the glottis, further the meninges, and above all, the serous membranes are greatly disposed in the nephritic to become the seat of severe serous, fibrino-serous, or even *purulent* inflammation. If you meet *post mortem* with a purulent peritonitis, in the absence of a puerperal cause and without perforation of the digestive tract or one of the other known causes of the disease, I can only urge you to attempt to discover whether the patient had not suffered from a chronic simple or amyloid nephritis. But of all the disturbances setting in during the course of nephritis, none has been more discussed than so-called *uræmia*. By this is meant a series of nervous symptoms, which differ somewhat according as the condition appears *acutely* or develops slowly, *chronically*. In the acute form—to select at least its most marked characteristics—the patient, perhaps after violent headache and vomiting, or without any precursors, suddenly loses *consciousness* and is attacked by epileptiform *convulsions*, which, after continuing for a while, are succeeded by deep coma; from this coma the patient passes, as a rule, into a fresh attack of clonic spasms, and thus a series of convulsions may ensue, till finally death takes place in the most profound coma. Yet it is rather unusual for patients suffering from renal disease to perish during the first uræmic attack. They generally recover, and it may happen, especially in acute nephritis, that the first is also the last attack during the whole life; or after a time a fresh invasion occurs, which they also survive, and later a third and fourth, and so on; but in the end these patients perish in a seizure, unless life is previously destroyed by a hæmorrhage into the brain or by one of the intercurrent inflammations. These severe irritative phenomena are usually completely absent in the chronic form of uræmia, or the convulsions, which are often so terrible, may be represented merely by twitchings of single muscle-groups. But no improvement in the course of the disease takes place in consequence. On the contrary, the moroseness, drowsiness, and indifference, which are the earliest symptoms in the patients in question, develop slowly and gradually, but steadily, into more and more marked apathy and somnolence, and finally pass into a coma no less profound than that which in the acute uræmic seizure envelops the patients between and after the convulsions; and in this state of stupefaction, which may last uninterruptedly for a number of days, they probably perish without exception.

But the fact that these various disturbances are so frequently observed during the course of nephritis does not certainly establish their dependence upon it, to say nothing of clearing up the mode of this dependence. Indeed, in view of the very different forms of nephritis with which you have become acquainted, and the very dissimilar effects which they exert upon the function of the kidneys, you will probably from the start have entertained serious doubts as to whether the reaction of the organism will be the same towards disturbances so diverse in their nature. Is it really equivalent to the body whether the amount of urine passed in the twenty-four hours is greatly reduced—as in acute nephritis or the butter-kidney—or abnormally increased, as in the purely chronic nephritis leading to contraction? Or is it a matter of indifference whether the excretion of solid urinary constituents accurately corresponds to their daily production or falls short of it? Nephritis has a varying significance as regards the urinary secretion, and how can its action on the organism generally be always the same? Now, after we had learned to differentiate the various forms and to accurately define the questions involved, it soon became apparent that the great majority of the morbid disturbances just mentioned are met with only in those renal affections which are accompanied *by a diminution in the volume of the urine and a falling-off in the excretion of solid urinary constituents.* Such are acute nephritis and those cases of chronic inflammation in which a compensatory rise of blood-pressure and cardiac hypertrophy either fail to take place, as in the amyloid, or again disappear, as in contracted kidney with disturbance of compensation; and, of non-inflammatory affections, bilateral stenoses or obstructions of the ureters, impermeable strictures of the urethra, and in general all those processes which prevent or seriously interfere with the discharge of the urine from the body; and, lastly, cholera and eclampsia, both having this feature in common, that the urinary secretion is greatly diminished or even completely arrested.

However strong, accordingly, is the probability that these morbid symptoms are but the effects of the inadequate removal from the body of the urine and its constituents, you will yet desire that this conclusion should be confirmed by experimental proof that the suppression of the urinary secretion is followed by analogous conditions in animals. Whether the retention of urinary constituents be produced by *ligature of the renal arteries*, by *extirpation of both kidneys*, or by *tying both ureters*, or again by a combination of two of these procedures, does not in principle make much difference; for it is obviously immaterial whether the urinary constituents remain in the blood or re-enter it after excretion. As regards certainty of results, however, ligature of the renal arteries is inferior to either of the other methods, more especially in the dog, whose kidneys are sometimes supplied by very considerable collateral arteries which enter it at the convexity; and since, on the other hand, extirpation of the kidneys involves a much more severe injury than does ligature of the ureters, this latter procedure seems to me best adapted to our purpose; moreover, you will think it no disadvantage that the effects are less stormily developed after this operation, so that more time is allowed for observation. *All animals perish as the result of bilateral occlusion of the ureters*, yet after unequally long intervals; rabbits succumb, as a rule, after two or at most three days, while dogs may remain alive for four, five, or even six days. The effects of the retention of urine *increase continuously* as time goes on. While, after an operation carried out as gently as possible, the animals display no marked symptoms during the first few hours, but run about briskly and eat and drink with appetite, this state of well-being usually gives place even during the first day to a certain languor and *malaise*. The animals sit or lie cowering in a corner, drink little, and more especially refuse absolutely to eat. In dogs, *vomiting* usually occurs on the first day, but certainly on the second; from this time it is frequently repeated, causing the ejection of all fluids taken by them. Rabbits, on the contrary, being unable to vomit, are attacked at the same period by violent *diarrhœa*, a symptom which, in dogs with their profuse vomiting, only rarely occurs or may be completely absent. After some time, which, you will note, is usually longer the more copious the vomiting or diarrhœa, the animals become increasingly apathetic and drowsy and gradually fall into a somnolent condition, which in rabbits is occasionally interrupted by slight twitchings, in dogs by marked convulsions. Finally, the animals can no longer be roused out of their deep coma, and die without the accession of new symptoms.

In these experiments on animals, you do not, it is true, meet with all the pathological events, which are observed in human beings suffering from renal disease; yet the most striking of them, namely the digestive disturbances and severe nervous symptoms, agree so closely in both, that it is impossible to admit a doubt as to their dependence on the retention of urine. But what is the nature of the actual connection between the retention and these symptoms? By what means does the retention give rise to disturbances of the digestive apparatus and nervous system? Unquestionably, the idea most obviously suggesting itself was, and is now, to attribute to the retained urinary constituents a kind of *poisonous action*, which is the more marked the greater the accumulation of materials in the blood, or the longer the retention lasts. That such an accumulation actually occurs has long been known, and improved methods of chemical investigation have afforded most positive confirmation of the fact, at least with regard to that substance which is present in sufficient quantity to at all admit of trustworthy quantitative estimation, *i. e.* the *urea*.* After extirpation of the kidneys or ligature of the ureters in dogs and rabbits, urea may be detected in all the organs and fluids of the body, in quantities which are greater in proportion to the time that has elapsed since the operation. Almost the same amount of urea has, under certain circumstances, been obtained from the organism as would during the same period have been excreted by the animal in the urine ;* and if usually the amount accumulated in the body more or less falls short of that calculated to be produced but not excreted through the kidneys, this is very simply explained by the removal in the vomited matters or stools of a quantity of urea, either undecomposed or as ammonium carbonate. Many investigators have succeeded, in complete accordance with these results, in demonstrating the presence of urea in the blood and serous fluids of renal and cholera-patients, &c. As to the importance of the accumulation of urinary constituents for the animal experimented on, this appears to me to be clearly indicated by the fact just mentioned, that the severe nervous symptoms which always usher in the fatal result, are later in appearing the more of these constituents has been removed from the body *per os et anum.*

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* Cf. especially Voit, 'Zeitschr. f. Biolog.,' iv, p. 116, *et seq.*, which also contains a critique of all the older statements.

Yet this interpretation was capable of being tested by direct experiment, which has apparently decided against it. If it be really the retained urinary constituents that call forth the symptoms generally termed "uræmic," these symptoms must also be produced by the direct introduction of the substances in question into the blood. Now a number of writers† have succeeded in convincing themselves that neither the infusion of pure filtered urine—even when obtained from another species—nor the injection of urea or sodium urate is attended by any injurious results and produces no pathological symptoms, even when such quantities of the latter are injected as could not accumulate in the blood during a retention of several days' duration. The result of the injection is simply that the volume of the urine and quantity of urea excreted are very soon increased and continue abnormally abundant till the substance introduced is removed from the body. Moreover, if blood be transfused into the vascular system of a healthy dog from one rendered uræmic by ligature of the ureters, no grave disturbance follows.[*] Lastly we have to take into account some additional experiences, which show that the accumulation of urea in the body is far from always increasing *pari passu* with the severity of the uræmic phenomena.[†]

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* Cf. Voit, 'Zeitschr. f. Biolog.,' iv, p. 116, *et seq.*

† Cf. Frerichs, 'Die Bright'sche Nierenkrankheit,' p. 106.

These were the reasons that gave occasion to the enunciation of another theory, which Frerichs more especially has sought to establish by an experimental investigation,[‡] now grown famous. According to it, the urea is not *per se* a poison, but only becomes so on being converted in the vascular system into ammonium carbonate, under the action of an appropriate ferment, which, though not always present in the blood, may under certain circumstances originate there very rapidly; to the ammonia is ascribed that baneful potency which produces the uræmic disturbances of function. We may fairly dispense with a minute exposition of the reasons by which Frerichs sought to support this his theory, since the doctrine, eagerly adopted at first, but since then the subject of many a dispute, now possesses a purely historical interest. For neither the theoretical conception nor the facts themselves have proved to be tenable. By means of exact quantitative experiments, Voit[§] has shown that the urea of the blood and tissues of the *living* organism is not transformed into ammonium carbonate, and that even when its conversion has begun in putrefying blood, its progress is very slow, much slower in particular than the putrefaction: only in *one* region of the body does the conversion of urea take place rapidly, namely the *intestine*, but here the ammonium carbonate always produces local effects and never gives rise to general uræmic phenomena. It is true that when injected in sufficient doses directly into the blood, the ammonium carbonate may bring about convulsions and coma, and thus give rise to a complex of symptoms which in some of its most essential features closely agrees with that of acute uræmia.[‖] Nevertheless—and this is the second principal

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[*] M. Bernhardt, 'Qua in re uræmiæ natura posita sit,' I.-D., Berlin, 1866.

[†] Vide Voit, loc. cit., p. 156; Bartels, loc. cit., p. 116.

[‡] Frerichs, 'A. f. physiol. Heilkunde,' x, p. 399; 'D. Bright'sche Nierenkrankheit,' p. 107.

[§] Cf. Voit, 'Zeitschr. f. Biolog.,' iv, p. 116, *et seq.*

[‖] Rosenstein, 'Virch. A.,' lvi, p. 383.

[illegible] Frerichs' theory—it has been proved that all the statements formerly made as to the presence of ammonia in the blood and expired air of animals deprived of their kidneys, or of uræmic persons are erroneous. Ammonia can only be detected—and even then not always—in the vomited matters and diarrhœic stools. There is not a particle of evidence to show that it is ever present in the blood and [illegible] under these circumstances. It is evident, accordingly, that the modification of the ammonia-theory formulated by [illegible]* has also become untenable. According to this writer the supposed transformation of urea does not take place in the blood but in the intestine, or even in the urinary passages, while the ammonium carbonate enters the blood as such.

But if these chemical theories have apparently proved inadequate to explain the uræmic symptoms, no better fortune has attended the attempts made at approaching the problem from other standpoints. A number of writers who have [illegible] the most [illegible] of all the uræmic disturbances, the nervous symptoms, have sought their cause in inflammatory alterations of the meninges of the brain, or in [illegible] of the cerebral vessels, and then [illegible] these partly [illegible] and partly [illegible] views. A [illegible] theory, which recognizes the [illegible] in the [illegible] of hydræmia [illegible] in cases of [illegible]. [illegible] a sudden rise of [illegible] substance, [illegible] produces [illegible]. Now, although [illegible] has attempted to support this theory by experiment [illegible] it will be [illegible] of the [illegible] and [illegible] of water through the [illegible] specially [illegible] that the [illegible] should become [illegible].

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* [illegible]

† [illegible] London, [illegible]

‡ [illegible]

§ [illegible]

Nevertheless, you have yourselves seen that after the infusion of enormous quantities of a ·5 per cent. salt-solution into a vein, the brain with its membranes remains no less dry than in a healthy and normal dog—although the arterial blood-pressure has continued for hours at the highest normal values ever observed. It is incorrect, as I have repeatedly told you, that hydræmic blood transudes more readily through healthy vessels than does blood of normal composition, a statement which holds equally, whether the arterial pressure be high or low. Still less have we any need to examine into the correctness of Traube's view with regard to the implication of the large or mid-brain, if for no other reason, because the fact itself is far from being so certainly established as the framer of the theory believed. For while it is quite true that the brains of persons who have died during an attack of uræmia are sometimes found to be moister than usual, it is useless to discuss the causes and mechanism of the œdema—*since it is anything but constantly present in uræmic individuals.* Rather I can most positively assure you that, during the two decades which have elapsed since the appearance of Traube's publication, I have examined many brains in uræmic cases which were not in any way distinguishable as regards moisture from the normal. Hence the œdema of the brain, even if it had existed *intra vitam*,—on which point the post-mortem appearances give no reliable evidence—can only at most be an associated phenomenon, but not the cause of the uræmia.

But is it really so clearly established that the overloading of the blood with urinary constituents is an absolutely uninjurious condition? Is this actually demonstrated by the fact that urine or solutions of urea, &c., when injected into the blood, pass through the body without any bad result? By such a mode of procedure, a lasting excess of urinary constituents can never be produced; and if the injection of urea is to lead to absolutely certain conclusions, it is evident that the organism must at the same time be deprived of the power of excreting the urea introduced. As a matter of fact, a very different result was arrived at by experiments, when the chief channel of urea-excretion was occluded by ligaturing the ureters. After injections of uræmic blood, Bernhardt's dogs very soon developed the symptoms of severe illness and died much more rapidly than is customary after ligature of the ureters. Most experimenters, however, have found, on a detailed examination as to which are the really active and injurious substances of the uræmic blood, that animals with ligatured ureters or extirpated kidneys do not strikingly react to small doses of urea; but *after the introduction of larger quantities they perish with more or less stormy symptoms.* And in this connection it is necessary to remember that a not inconsiderable amount of urea may be removed by vomiting or diarrhœa, so that should *acute* nervous symptoms fail to set in after injections of urea into animals deprived of their kidneys, this would not absolutely disprove the danger of accumulations of urinary constituents in the blood. On the contrary, the appearance of vomiting and diarrhœa in these cases appears to me to clearly show that the overloading with constituents of the urine is far from being a matter of indifference to the body. This is demonstrated in a peculiarly striking manner by an ingenious experiment of Voit.* A small dog weighing three kilograms which was supplied in its food with more than eighteen grams urea, excreted the entire quantity during twenty-four hours together with a profusion of urine, provided it received an unlimited supply of water; when, however, after the same dose of urea, the little animal was deprived of all fluids, it became languid after a few hours and soon developed violent vomiting which was repeatedly renewed on the same and following days; the matters first vomited were acid, later on strongly alkaline, and then gave off a copious visible vapour on bringing a glass rod moistened with hydrochloric acid into proximity to them. Meanwhile the dog grew steadily weaker and more apathetic, got muscular twitchings and cramps, and in fact lapsed into an extremely critical condition; from this, however, it completely recovered when, water being given, a copious secretion of urine set in. You see, then, that although really large quantities of urea pass through the body without harm, their accumulation in the blood while the possibility of excretion is in abeyance may be accompanied by the most serious results. Yet later experimenters are, it is true, less disposed to admit the accumulation of *urea* to be the active cause of the uræmic poisoning. Thus, Astaschewsky* observed that a dog, with ligatured ureters, into which he introduced by the v. femoralis the whole of the urine passed by it in three days, in concentrated form, became restless, was attacked by vomiting with acceleration of the pulse, soon developed terrible convulsions, and died comatose 100 minutes after the injection; on the other hand, he failed to produce any uræmic symptoms by injecting urea, *even in enormous quantities;* vomiting and diarrhœa alone set in, but even these were rather late in appearing, and death was not hastened thereby nor by the injection of kreatinin. Much more destructive effects are believed by Astaschewsky, on experimental evidence, to be produced by the *mineral* constituents of the urine, in particular by the *salts of potash*, the importance of which in uræmic blood-poisoning had previously been pointed out by Voit. Under these circumstances while the active principle, in the strict sense, of uræmia is still an unsettled question, and it is possible even that different substances may produce the pernicious effects on different occasions, it will obviously be best to attribute the origin of the phenomena here occupying us, not to this or that ingredient of the urine, but generally to the retention of all its *solid constituents.* The factor preventing excretion is of little moment. The effect produced in Voit's experiment by want of water —without which the excretion of urea by the kidneys cannot take place—is brought about in almost analogous fashion by the inspissation of the blood in the choleraic seizure; other causes, again, are at work in the production of the anuria or oliguria in the paroxysm of eclampsia, in acute and chronic nephritis, and in the various impediments occurring in the interior of the urinary passages; yet as regards the effects of the accumulation of urinary constituents in the blood, the result is always the same. Moreover when, as is not so rarely observed,† renal patients treated by diaphoresis, suddenly develop uræmic symptoms after the very rapid absorption of large dropsical effusions, these are probably most simply explained by the rapid overloading of the blood with the urinary constituents contained in the dropsical fluids; for on the urinary secretion afterwards becoming abundant, the threatening symptoms speedily disappear.

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* Cf. Voit, 'Zeitschr. f. Biolog.,' iv, p. 116, *et seq.*

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* Astaschewsky, 'Petersbg. medic. Wochschr.,' 1881, No. 27. Identical results were arrived at by Feltz and Ritter, 'De l'urémie expérimentale,' Paris, 1881.

† Bartels, loc. cit., p. 122.

The real test of the correctness of the view here developed would consist in its affording a plausible explanation of the entire phenomena of uræmia; and it is the more incumbent upon us to consider this problem, since the variety of the uræmic symptoms has been made use of by a writer of eminence* as an objection to the view of the unity of uræmia and of the uræmic morbid poison. I do not deny, of course, that the uræmic phenomena may be displayed by very different organs; indeed, I have myself hastily sketched some of these variations; it is true also that the symptoms are not all observable in every case. A possible explanation of such differences has just been hinted at. Without any real necessity, however; for experience teaches with regard to every disease that the various symptoms occur irregularly, and the only question therefore is,—Do the individual cases actually present groups of symptoms so different as not to be reconcilable? Now, the principal difference here consists merely in the *rapidity* with which the symptoms are manifested, and, in dependence on this, their severity; the more rapidly they set in, the more stormy will be their course; the longer they are absent, the more, as already described, will the irritative phenomena be obscured by those of depression. This difference does not, however, elude explanation. For it is the very natural result of *a rapidly or slowly culminating overloading of the blood with urinary constituents.* What are the circumstances in which we observe attacks of *acute* uræmia, such as are usually ushered in by violent vomiting and often by sudden amaurosis, and which are characterised by convulsions and coma? We observe them as the result of rapidly established impermeability of the urinary passages or of a sudden incapacity to discharge the urine secreted; next in an extremely typical form, in eclampsia parturientium or gravidarum; further in some cases of so-called cholera-typhoid; but acute uræmia is decidedly most common in the course of non-suppurative nephritis, both in the acute and chronic forms. Of these different categories, the first in a measure repeats the experiment of bilateral ligature of the ureters; in eclampsia, it is the vascular spasm of the small renal arteries—which appeared so plausible to us—that in a moment gives rise to the retention of the urinary constituents in the blood; in the train of cholera, uræmic complications occur only when the urinary secretion has not been re-established, so that the urinary constituents retained in the blood since the attack consequently fail to be excreted; and, lastly, that acute nephritis gives rise in the briefest space to an extreme reduction of the urinary secretion, you already know. But how as regards chronic Bright's disease? Here oliguria is out of the question, to say nothing of its sudden development; on the contrary, in chronic nephritis the quantity of urine secreted may for months and years continue perfectly normal, and may often enough be excessive. And yet it is precisely in these cases of chronic nephritis that most exquisitely acute uræmic attacks occur, and in particular it is in them that the attacks are repeated as time goes on. Despite this apparent contradiction, the connection of cause and effect is the same. For the excretion of the urine and its constituents in chronic nephritis proceeds in a regular manner only so long as the heart works with abnormal vigour. When the heart begins to fail, oliguria and with it retention of the urinary constituents occurs in these cases also. Now, it is an old experience that the uræmic attack even in cases of chronic nephritis is *almost always preceded by a reduction of the urinary secretion*, which itself, as a rule, depends on a disturbance of compensation of the hypertrophied heart. This, I believe, supplies the key to the paroxysms occurring during the course of chronic Bright's disease. So long as the heart continues to meet the demands made upon it, the excretion of urinary constituents is perfectly adequate, and, despite the nephritis, the patients feel quite well, or they exhibit certain pathological symptoms, though no evidence whatever of uræmia. But from the moment when, for any reason, the functional power of the heart is reduced, retention of the urinary constituents is unavoidable and the danger of uræmia arises; when there is a rapid falling off in the work of the heart, the signs of acute uræmia, *the uræmic paroxysm*, rapidly develops, sometimes even more rapidly than the mechanical œdema. Since, however, the cardiac insufficiency may again pass off, the uræmic attack may be perfectly recovered from, though of course the danger of a recurrence of the symptoms is not thereby averted. That this is actually the connection of events is best taught by the state of the pulse of the patients in question. For the paroxysm is, as a rule, preceded by a short period during which the pulse is often considerably retarded, and during the attack itself it is frequent, *small*, and even *imperceptible to the finger*, or it can be seen and felt only over the heart and carotid.* That exceptions to all this are met with, I am well aware. Yet it does not appear to me especially remarkable that, during the paroxysm itself, with its violent and long-continued convulsions, a considerable increase of blood-pressure should under certain circumstances take place; it is, in fact, no more remarkable than the occasional rise of temperaturé, and may even be regarded as a kind of self-regulation by the organism. It is also very possible that a rapid reduction of the urinary secretion in chronic nephritis may occasionally be due to some other cause than weakness of the heart; and if in rare but well-accredited cases the urine has not been diminished before the appearance of the convulsions, but has been excreted in at least the normal quantity, it still continues questionable whether the amount of solid urinary constituents was also unreduced—and on this everything depends. All things considered, such exceptions should, in my opinion, only stimulate us to inquire into the pathogenesis of the uræmic attack in the individual cases, but should not lead us to doubt our well-founded theory, supported as it is by the great majority of observations.

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* Rosenstein, 'Virch. A.,' lvi, p. 383.

You perceive once more what an important *rôle* is played by cardiac hypertrophy in the history of nephritis; by its presence a rapid overloading of the blood with urinary constituents is made possible, or at least greatly facilitated in chronic nephritis also, so that acute uræmic paroxysms may appear in consequence. Where an adequate hypertrophy of the heart is not established, no matter what the cause of its absence, the progress of a chronic insidious nephritis will, it is true, be attended by an accumulation of urinary constituents in the blood, but only by a *slow* and *gradual* one. In these cases, as a matter of fact, true paroxysms of uræmia are usually completely absent, despite the extreme oliguria which often continues for months. It has been repeatedly and correctly stated by experienced clinicians, in particular by Traube, that uræmic paroxysms are extremely rare accidents in amyloid nephritis more especially; and in truth, nothing of the kind has been observed except in the rare cases of amyloid contracted kidney accompanied by cardiac hypertrophy: observations, which for the rest are sufficient of themselves to disprove, were it necessary, the view which would see in the amyloid change a direct obstacle to uræmic intoxication. The explanation is to be found, as you at once perceive, in a very different direction. It is not because of the presence of amyloid degeneration that we miss the uræmic paroxysms, in the history of waxy and butter kidney, but because the heart does not in these forms undergo hypertrophy; and if, despite the amyloid degeneration, hypertrophy of the heart be present, a rapid accumulation of urinary constituents in the blood may under certain circumstances occur, and the preliminary conditions and cause of the uræmic attack be in this way established. For, as you will carefully note, it is only the *acute* uræmic paroxysm that is such a great rarity in amyloid kidney; the symptoms of chronic uræmia are far from uncommon in amyloid nephritis, and would certainly much more frequently close the scene, did not various inflammatory and other processes, soon to be discussed, still earlier terminate life. The picture of chronic uræmia, as above described, is consequently more frequently observed in *bilateral hydronephroses*, which depend on gradually developing stenosis of the ureters, and are accompanied by a slow but steadily increasing oliguria, than in subacute and chronic nephritis without cardiac hypertrophy.

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* Cf. *e.g.* Wagner, 'M. Br.,' p. 63.

Nor can the connection between the *digestive disturbances* and the uræmia fairly be questioned. Not that every attack of vomiting or diarrhœa in renal disease is uræmic in its origin! When vomiting occurs in a person, in one of whose ureters a calculus has become fixed, it is due to the same reflex which is at other times initiated, for example, by an impacted gall-stone, and obstinate diarrhœa in a patient with large waxy kidneys may very often be referred to the simultaneous presence of amyloid degeneration of the intestine. But even if these cases be neglected, various dyspeptic disorders are some of the very commonest symptoms of those renal diseases under the influence of which the excretion of urine is abnormally reduced, and, like the nervous uræmic phenomena, they set in with greater violence in proportion to the rapidity with which the overloading of the blood with urinary constituents has been brought about. Violent vomiting, as has been mentioned more than once, usually precedes the uræmic paroxysm; moreover, the organism is wont to react by vomiting to the retention of urinary constituents still earlier than by nervous symptoms, so much so that the latter may even be held in check, or at any rate deferred by the copious emesis. As a matter of fact, this vomiting relieves the body and its juices of the accumulated urinary constituents; nevertheless I should hesitate to regard it as a kind of vicarious excretion by the gastric mucous membrane. Though I am perfectly conscious that the mechanism of these processes is far from being fully cleared up, still everything appears to favour the idea that the uræmic vomiting is *central.* The easily diffusible urinary constituents, above all the urea, pass into most of the secretions, amongst others into the gastric juice and the digestive juices which are poured out into the intestine, but the urea present in the stomach does not give rise to the emesis; the vomiting centre is directly stimulated by the blood which is overloaded with urea, and causes the ejection of that present in the stomach along with its other contents. That this is the connection of events, in my opinion follows conclusively from Voit's experiment, in which a dog was given urea by the mouth; for the vomiting, far from ensuing rapidly—at the time, that is, when the substance was contained in greatest abundance in the stomach—took place only when a considerable quantity had passed into the blood by absorption. The urea, while undecomposed, is no more capable than are the other urinary constituents of giving rise to vomiting by direct irritation of the gastric nerves, and that it is always at once converted in the stomach into ammonium carbonate is simply a myth. After ligature of the ureters, the matters vomited during the first few days have constantly an acid reaction, and only during the period preceding death can ammonium carbonate as a rule be detected therein. In nephritis also the reaction of the vomit is mostly acid, and many investigators have obtained undecomposed urea from it; the much-vilified penetrating ammoniacal odour is only rarely given off by the vomited matters, except in the most severe uræmia due to renal disease, where the patient lies in profound coma. Voit's experiment teaches further that the retention of water is not responsible for the vomiting. Bartels, in conformity with his other views, was ready to attach great importance to the retention of water as a cause of vomiting, and believed that he had repeatedly convinced himself that the gastric mucous membrane shared in the nephritic œdema, and thus gave rise to the emesis. Yet to say nothing of the doubt as to whether œdema of the mucous membrane of the stomach can possibly be productive of vomiting, this localisation of it is at any rate extremely uncommon, and for the great majority of cases, *e. g.* the emesis of acute nephritis, and that occurring during the uræmic paroxysm in chronic Bright's disease, we must unconditionally reject this explanation. The condition of things is less clear in the *diarrhœa* of renal disease, a less common symptom than vomiting. A more important part is certainly played here by the decomposition into ammonium carbonate of the urea excreted into the intestine, if for no other reason, because the alkaline reaction of the small intestine is much more favorable to the process. Moreover, diphtheritic enteritis is a comparatively frequent discovery in persons who have perished from chronic nephritis; it chiefly attacks the cæcum and ascending colon, and may unhesitatingly be referred to the corrosive effects of the ammonia. Still, diarrhœa of a non-dysenteric character often occurs in nephritis, and can no more be attributed to the action of the ammonia than can the purging which so rapidly follows ligature of the ureters in the rabbit. We are as yet unable in these cases to accurately define the mechanism by which the augmented peristaltic action is brought about; yet you will hardly go astray, I think, if you regard the *accumulation of urinary constituents in the blood* as the real determining factor in this instance also. When the accumulation takes place rapidly, violent vomiting is the result, and in rabbits, as well as sometimes in man, profuse diarrhoea. When the accumulation is gradually developed and persistent, the vomiting may be repeated daily for weeks and months; a slight but obstinate diarrhoea may also occur, and the patients complain incessantly of want of appetite, nausea, and various dyspeptic symptoms.

That the *pruritus of the skin* in renal disease depends on the accumulation of urinary constituents in the blood, appears extremely probable to me, in view of the fact that it is invariably associated with serious nervous symptoms of uræmic origin. The same thing undoubtedly applies to the severe *asthmatic paroxysms*, while the *less intense dyspnœic troubles* of which patients with chronic nephritis have so frequently to complain, must probably be attributed to the enlargement of the heart. As regards the tendency to hæmorrhages, it is evident that they cannot simply be referred to the uræmic blood-poisoning, inasmuch as an accurate analysis of individual cases shows that the hæmorrhagic diathesis and the urinary retention are far from running parallel. No hæmorrhage occurs in acute nephritis, in chronic inflammation unaccompanied by cardiac hypertrophy, and more especially in large waxy kidney; the form of renal disease in which it is chiefly observed is *chronic nephritis with hypertrophy of the heart.* Persons with typical contracted kidneys are those most liable to perish as the result of copious hæmorrhage into the brain, and it not uncommonly happens that they more especially are attacked by apoplexy while in a condition of perfect well being, and before the renal disease has betrayed itself by a single symptom. But even when a person well known to be suffering from Bright's disease gets an apoplectic seizure, this accident does not usually occur during a period in which compensation is disturbed, and we are therefore likely to be correct in regarding an abnormal rise of arterial pressure as the cause of the cerebral hæmorrhage. The vessels that rupture are not, of course, healthy; they are the arterial branches which in all persons over a certain age so frequently become the seat of aneurysms or atheromatous disease, and are unable to withstand the high internal pressure; in this way it becomes intelligible that the cerebral hæmorrhages of the nephritic are wont to occupy the same regions which are the characteristic seats of the apoplexy depending on old disease of the vessels, *i. e.* preferably the *corpora striata and thalami optici.* Yet these bulky hæmorrhages of the nephritic do not constitute the real difficulty; it is rather those bleedings in which a ruptured vessel cannot be discovered that elude explanation. I refer to the *punctiform hæmorrhages* which are sometimes found scattered in very large numbers over the entire *brain* in persons who have died in or after a uræmic paroxysm, further to the *bleedings of the retina* in retinitis albuminurica, and lastly to the *hæmorrhages*, sometimes several times repeated, *from the nose, stomach, and intestines.* Of these, the punctiform retinal hæmorrhages have given rise to most investigation and discussion, but precisely here the question is complicated by the other remarkable changes always present in specific retinitis albuminurica.* These changes consist—to select at least the main features—*in white spots and streaks*, from the most minute specks to *plaques* as large as the papilla, which in both eyes surround the papillæ and are usually most numerous and closely aggregated at the temporal side. In the most severe cases, the papillæ are at the same time clouded and swollen, and during the subsequent course of the affection the whitish plaques spread and coalesce repeatedly with one another, while the loss of acuteness of vision, with which the retinitis commenced, goes on steadily increasing. However characteristic and well-known these appearances are, we have not yet obtained an accurate insight into the development of the disease and the conditions of its origin. True, ophthalmologists have accurately followed the course of the affection in innumerable cases by the aid of the ophthalmoscope, and we are consequently better acquainted with this retinitis than with many other chronic processes—knowing as we do, that it, as a rule, begins with extreme hæmorrhagic hyperæmia of the retina, that white spots subsequently make their appearance, at first isolated and very minute, but constantly increasing in number and size, while the hyperæmia become retrogressive. Nor is there any want of careful microscopical investigations, by which the white patches have been shown to depend mainly on a more or less dense deposit of compound inflammatory corpuscles in the two molecular and inner nuclear layers, as well as on a peculiar, sometimes more even, at other times more varicose, *hypertrophy and* [illegible] *of the non-medullated fibres* of the nerve-fibre layer. Nevertheless the actual anatomical genesis of the process is obscure, and we allow ourselves to be influenced more by certain general impressions than by definite anatomical or clinical signs in interpreting the entire process as an inflammatory one, and in applying to it the name, retinitis. As regards the pathogenesis of this retinal affection, however, there is certainly not the remotest doubt that it *depends directly on the nephritis*; it has never been met with in the absence of renal disease, and an already advanced retinitis has repeatedly been observed to recede and even to completely heal as the nephritis improved. But in view of the dissimilar disturbances undergone by the renal function under the influence of a nephritis, this fact alone is not a great addition to our knowledge, and you will certainly ask at once, in what form of renal inflammation does the retinitis occur? As regards this point, all observers, from the time the affection was first recognised down to the present day, are agreed that in the vast majority of instances retinitis albuminurica occurs during the course of *chronic nephritis associated with cardiac hypertrophy*. So much is this the case that, at a time when the retinitis had been known for a number of years, Traube and Graefe declared that they had never met with an instance in which hypertrophy of the heart was absent,* and if since then the hypertrophy has not been detected in a few cases of fresh retinitis, these were always instances of primary or secondary acute or subacute nephritis, which were too recent to have brought about the cardiac change, but were yet by their nature well adapted to do so. For the rest, these cases in which the retinitis is observed in such early stages of the renal disease, are the very rare exceptions; in the enormous majority of all acute inflammations of the kidneys, the retina shows no trace of the specific alterations. It also escapes in chronic nephritis unassociated with cardiac hypertrophy; thus it is never affected in cases of large waxy kidney, while the disease has several times been seen, by Traube amongst others, in amyloid contracted kidney with hypertrophy of the heart. As you perceive, the retinitis of Bright's disease displays certain analogies in its appearing with the uræmic paroxysms, which like it are so extremely frequent in chronic nephritis associated with hypertrophy of the heart, and practically do not occur in the absence of hypertrophy. Nevertheless, the retinitis and the uræmic paroxysms cannot be due to the same cause; for the paroxysms form an integral feature of the picture of acute nephritis as well as of sudden suppression of the urinary secretion generally, while though uræmic amaurosis does occur in these cases, retinitis albuminurica does not. The latter is a conspicuously *chronic* affection, and cannot consequently be induced by rapid overloading of the blood with urinary constituents. Yet a connection between it and chronic accumulation of the urinary constituents in the blood is equally impossible, since it is also absent in cases of chronic uræmia. Thus in spite of all our scruples on *a priori* grounds, we are obliged, like Traube, to have recourse to the cardiac hypertrophy and high arterial tension, and to regard them as at least very potent factors in its production. I do not conceal from myself the various objections to which this view is open. If the hypertrophy of the heart and the high arterial pressure actually bring about the conditions necessary to the development of the retinal disease, why is such disease never observed in other forms of so-called idiopathic hypertrophy, *e.g.* in nervous cor bovinum? And then, how are we to conceive of the production of this retinitis on the basis of the high arterial tension? To regard the retinal hæmorrhages as the primary effect is scarcely legitimate, because, though we observe such hæmorrhages in other conditions, they are never followed by the highly characteristic degenerations; moreover the affection does not begin with simple hæmorrhage but with a more or less extensive *hæmorrhagic hyperæmia* of the retina.

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* Cf. Leber, 'Krankheiten der Netzhaut,' Leipsig, 1877, p. 572.

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* Traube, 'Ges. Abhandlungen,' ii, p. 985.

On the other hand, in the bleedings taking place in the nephritic from the nose and gastro-intestinal canal, we have to do, not with hæmorrhagic inflammations, but simply with true hæmorrhages; yet as regards the conditions on which these depend, we are equally in the dark. We do not even know whether they occur *per rhexin* or *per diapedesin!* That the attacks are acute is beyond question, especially as regards the epistaxis; and since, so far as I know, they occur only during the course of chronic nephritis with hypertrophy of the heart, it is natural to draw a parallel between them and the cerebral hæmorrhages in this disease. Yet you will not look upon this idea as more than a suggestion having no greater value than the view which refers the punctiform hæmorrhages of the brain in the uræmic to the convulsions.

Though, as you perceive, we can hardly throw the responsibility of the so-called hæmorrhagic diathesis of the nephritic on the overloading of the blood with urinary constituents, there is much less objection to our accepting a connection of this kind in explanation of the tendency of the nephritic to *inflammatory processes*. For though no form of nephritis enjoys *per se* an immunity from these inflammations, yet they are wont to set in only when, as the result of the renal affection, the excretion of urine has for some time been abnormally reduced. Thus, it is something quite common for a pneumonia, or a phlegmonous erysipelas to bring about the fatal termination in acute nephritis; moreover, persons suffering from chronic nephritis more often die, in the stage of disturbance of compensation, from an attack of erysipelas, pericarditis, phlegmone circa glottidem or pneumonia than from a uræmic paroxysm, and in amyloid nephritis a peritonitis or bilateral pleuritis not uncommonly closes the scene; finally, the last weeks of life of patients with bilateral stenosis of the ureters are often disturbed by the occurrence of such inflammations: that all these inflammatory affections have a certain tendency to become purulent, I have already told you. Now, I am not, it is true, in a position to accurately state the mode of origin of these inflammations in the nephritic; still it appears to me to be thoroughly conformable to our other conceptions of the life of the vessels that we should ascribe to the accumulation of urinary constituents in the blood a pernicious effect on the condition of their walls, of such a kind that, on the one hand, trifling causes suffice to set up considerable inflammations, and, on the other hand, that inflammations however originating run in these patients a particularly severe course. It is possible that the retention not only of the solid urinary constituents in the blood but of the water as well may play a part here, that the inflammation is not merely *uræmic* but also *hydræmic* in its origin. It is scarcely feasible to distinguish between the two in nephritis, since the retention of the solid urinary constituents and water of the urine occur *pari passu.* Yet the fact that persons in whom hydræmia has been produced by some other cause are not attacked by such severe inflammations renders it probable that the chief stress should be laid on the uræmia, *i. e.* on the overloading of the blood with solid urinary constituents. If this be correct, you will now understand why I recently (vol. iii, p. 1292) raised the question whether some of the œdemas in renal disease should not be attributed to the retention of the solid urinary constituents in the blood. As regards œdema glottidis of nephritic patients, no one entertains a doubt, I think, as to its inflammatory nature; but who knows whether many an ascites, hydropericardium or anasarca setting in, say, during the course of an amyloid nephritis, is not of inflammatory origin, *i. e.* the product of a secondary uræmic inflammation?

SECTION VI.

THE PATHOLOGY OF ANIMAL HEAT.

CHAPTER I.

THE REGULATION OF TEMPERATURE.

Source of the blood-heat.—Means of regulation by which a constant bodily temperature is maintained.—Regulation in presence of altered heat-production and of variations in the temperature of the surrounding medium.—Regulation by increased production of heat when the external temperature is low.—Limits of the regulative capacity.—Tetanus.—Cooling and freezing.—Overheating.—Sunstroke.

Failure of regulation.—Deficient production.—Samuel's experiments.—Failure of the regulative mechanism by loss of heat.—Disturbances of the circulation through the vessels of the skin.—Cutaneous hyperæmia.—Varnishing and scalding.—Solutions of continuity of the spinal cord and other injuries of the central nervous system.—Experiments.—Explanation.—Rise of temperature during the agony.

Stadium algidum of cholera.—Post-mortem rise of temperature.

Not without good reason was it contrived that the human organism should in health possess an approximately constant temperature of about 37·2°, independently to a certain extent of the heat of surrounding objects. For this is the most favorable temperature as regards the activity of all the organs; all the bodily functions then take place most energetically, or, at any rate, in that manner which is best suited to the body and its purposes. That this is the case you have learned from physiology, and during the course of these lectures you have also on very different occasions become acquainted with deviations from the normal bodily temperature as causes of more or less severe disturbance of function. The conditions on which this constant temperature of the body depends are well known to you. For you are aware that *heat is* continually *produced* by the chemical processes taking place in the organism, and in such quantities on the average as would suffice to warm the body in half an hour by almost 1°, and consequently in twenty-four hours to 48°, *i. e.* to an elevation incompatible with life. That this does not happen is owing to the continuous *loss of heat* undergone by the organism; and it is the equilibrium between production and loss that secures the maintenance of the bodily temperature at an almost unvarying height. It is hardly necessary to tell you that production and loss are not evenly distributed over the body. Rather, we can point to a number of organs—chiefly the muscles and glands—as the essential seats of its production, while heat is lost principally from the surface and also from the lungs, owing to the evaporation and warming of the inspired air there taking place: the amount of heat removed with the urine and fæces is so slight as to completely fall into the shade. With such extreme and striking inequalities on the part of the various regions of the body, it would clearly be indefensible to speak of a definite bodily temperature, were it not that the equalisation of these differences is provided for by the conduction of heat from organ to organ and from tissue to tissue, and in a much higher degree by the circulating blood. The blood leaving the thermogenic organs is mixed with that returning from the skin to the interior, and since the blood with its temperature thus modified now flows through innumerable most minute and closely aggregated channels in every part of the body, the heat of the blood becomes the heat of the body. Still it is, of course, out of the question that all parts of the body should have a constant temperature of 37° approximately. In reality this applies only to the internal parts, which constitute, it is true, the greatly preponderating mass of the body, while the surface from which the continuous cooling takes place varies greatly in warmth, but is always cooler than the interior; between the two is an intermediate zone, in which gradual transitions occur from the higher temperature of the interior to the lower temperature of the exterior, a zone which is thicker in proportion to the amount of heat lost at the corresponding portion of the surface.*

That a definite constant temperature of the human organism should in this way be secured by the equilibrium between production and loss of heat is less remarkable than is *the maintenance of this constancy under very dissimilar internal and external conditions.* On remembering the extraordinary differences to which the heat-production is liable as the result of muscular exertion and of the consumption of food, and on considering how wide are the limits within which the loss of heat varies, according to the temperature and moisture of the surrounding medium, it is impossible to doubt that the organism must have command over very perfect *regulative mechanisms,* when, despite such variations, it can maintain its temperature constant. The body is in fact provided with the means of regulating both the loss and the production of heat, although the former are the more effective. They it is in particular that assert themselves promptly and energetically in opposition to *alterations in heat-production.* While the number of respirations in a resting and fasting man is moderate and his skin generally is pale, cool and dry, and supplied only by a moderate quantity of blood, all this is altered during digestion and especially during energetic muscular exertion; the respirations then become frequent, the skin more or less turgescent, a considerable amount of blood flows through the cutaneous vessels, and during violent exertion the skin is covered with sweat. All this has long been familiar to us without any real attempt having been made to accurately elucidate the mechanism by which the alterations are brought about. True, it has been determined by exact experiment that when the temperature of the blood is raised, the number of respirations and of heart-beats is increased; but the greater pulse-frequency is very far from involving, as you are aware, an acceleration of the blood-stream; and even were the increase in number accompanied by a strengthening of the heart's contractions, this would not secure that a larger quantity of blood should now enter the vessels of the skin. In order that this may occur, a *dilatation of the cutaneous arteries* is necessary, of which vessels I formerly told you that they even become narrowed against an increased rush of blood, provided the state of contraction of the circular muscular coat be not reduced by paralysis of the vaso-constrictors or excitation of the vaso-dilators. The rapidity and certainty with which the increased fulness of the cutaneous vessels appears on physical exertion accordingly render it probable from the outset that the change is the effect of nervous influences; but here we are met by the task of discovering the factor through which, when the production of heat is increased, the vaso-constrictors are thrown out of action or, as appears more probable from Heidenhain and Ostroumoff's investigations, the dilators are stimulated. This problem has recently been attacked by A. Fränkel,* who believes that he has discovered in the increased production of carbonic acid, which, as you know, accompanies both the consumption of food and muscular exertion, the factor causing excitation of the inhibitory nerves of the cutaneous vessels. But although he succeeded in raising the temperature of the skin of the extremities in some dogs, by causing them to inhale a mixture of gases containing carbonic acid, this result was far from constant; and since Fränkel himself very correctly points to several circumstances which might in this mode of experimenting unfavorably influence the results, it appears to me that the entire question is not finally settled by his investigation, however much the line of reasoning may have *per se* to recommend it. But although the question of the mechanism engaged is perhaps still open to discussion, the fact itself is securely established, and its value in the regulation of temperature is sufficiently obvious. For the loss of heat is not merely increased by that quantity which would correspond to the elevation of the heat of the skin depending on the general augmentation of heat-production, but the abundant flow of heated blood proceeding from the internal parts still further raises the temperature of the skin, and thus increases the loss of heat to the surrounding medium. The mode in which the increased heat-production gives rise to the *secretion of sweat* is still simpler. For the researches of Luchsinger* have taught us that the increase of the blood-heat constitutes a direct stimulus for the centre of the sweat-nerves. How great an amount of heat is withdrawn by the rapidly evaporating sweat need not be more particularly stated.

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* Cf. Rosenthal, 'Zur Kenntniss d. Wärmeregulirung b. d. warmblutigen Thieren,' Erlangen, 1872, p. 3, *et seq.*; further, in Hermann's 'Hdb. d. Physiolog.,' iv, 2, p. 381.

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* A. Fränkel, 'Zeitschr. f. klin. Med.,' i, Hft. 1.

Moreover, when the bodily heat is threatened *by very intense variations of the temperature of the surrounding medium*, the mechanisms regulating the loss of heat are brought into play. In a cold atmosphere the skin is pale, or, more correctly, pale bluish, and the cutaneous vessels are contracted, so that very little blood flows toward the surface; as a result, the skin soon acquires a temperature approaching that of the cool medium, and consequently the loss of warmth by conduction and radiation is essentially reduced. Conversely, the dilatation of the cutaneous vessels taking place in warm surroundings facilitates the loss of heat in a high degree, while, as already noticed, the high temperature calls forth a profuse secretion of sweat, which latter itself is attended by a considerable loss of heat, though the yield by conduction is reduced to a very small amount owing to the high temperature of the air. Human beings also have the means of aiding these regulative mechanisms not merely by wearing good conducting materials during the warm season of the year and by withdrawing heat by cold bathing, but more especially by confining the heat-production within narrow bounds through avoiding as far as possible all muscular exertion. In a cold climate, on the other hand, man clothes himself in poorly conducting materials and artificially heats his dwelling, while he seeks to increase his heat-production by consuming more food, and above all by vigorous movements and other muscular exertion. Such an augmentation of the heat-production is certainly an excellent method of keeping the bodily temperature at its normal elevation despite the increased loss of heat; yet it can scarcely be called a natural means of regulation by the organism. Such means, however, exist. I do not refer to the chattering of the teeth, the shivering and shaking by which a person is seized in the cold, but to *the increase of the metabolism* which takes place *in consequence of remaining in a medium of low temperature*. Since as early a period as the end of the last century, a number of writers[*] have assumed, on more or less convincing grounds, the occurrence of such a regulative increase; and at a more recent period Liebermeister[†] especially has declared himself emphatically in favour of the view; yet it cannot be claimed that the methods employed by himself and his pupils were adapted to convince us of the correctness of his ideas. Hence it happened that the objections raised by Senator, Winternitz and others[‡] to Liebermeister's conclusions were the means of greatly discrediting the regulative increase of production, till during the last few years a series of researches, in all respects exact, which have been carried out in the laboratories of Pflüger[§] and Voit[‖] have positively decided the question. At present it may be regarded as fully established that *when the surrounding temperature is low, the oxidative processes of the human body, as well as of warm-blooded animals, undergo a considerable augmentation*,—so long at least as the bodily warmth does not suffer through the external temperature. The animals on which the experiments in question were carried out—guinea-pigs were employed by Pflüger, cats by Voit—and also a man tested on the Munich respiration-apparatus showed, in a cold medium, increased absorption of oxygen and elimination of carbonic acid, which were pretty accurately proportional to the lowering of the external temperature. No voluntary movements took place during the experiments; indeed, their subjects behaved with such perfect quietness that nothing whatever of a remarkable kind was observed in connection with them. In which of the organs or tissues this plus-decomposition takes place has not as yet been certainly determined; yet many things go to show that we have here to deal with certain processes in the *muscles*, which are reflexly excited through the nerves conveying sensations of temperature from the skin, and which, though they do not lead to an alteration in the form of the muscles, set up a kind of *tension* in them.

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* Luchsinger, 'Pflüg. A.,' xiv, p. 369.

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[*] For a really complete summary of the researches bearing on this subject, see Voit, 'Zeitschr. f. Biolog.,' xiv, p. 57.

[†] Liebermeister, 'A. f. Anat. u. Physiol.,' 1860, pp. 520, 589; 1861, p. 28; 1862, p. 661; 'Deutsch. A. f. klin. Med.,' v, p. 117; vii, p. 75; x, pp. 89, 420; 'Volkmann'sche Vorträge,' No. 19; 'Handb. d. Patholg. u. Therapie d. Fiebers,' Leipsig, 1875, p. 215, *et seq.*; Gildemeister, 'Ueber d. Kohlensaüreproduction bei Anwendung kalter Bäder,' Inaug.-Dissert., Basel, 1870.

[‡] Senator, 'Virch. A.,' xlv, p. 351; l, p. 354; 'A. f. Anat. u. Physiol.,' 1872, p. 1; Jürgensen, 'Deutsch. A. f. klin. Med.,' iv, p. 323; Winternitz, 'Virch. A.,' lxvi, p. 503; 'Wien. med. Jahrb.,' 1871, p. 180; Murri, 'Lo Sperimentale,' 1873; Speck ('Med. Ctbl.,' 1880, No. 45) also questions that any influence is exerted by a cool bath on the oxidative processes of the body.

[§] Röhrig. u. Zuntz, 'Pflüg. A.,' iv, p. 57; Pflüger, ibid., xii, pp. 282, 333, xviii, p. 247; Colasanti, ibid., xiv, p. 92; Finkler, ibid., xv, p. 603.

[‖] Carl Theodor, Duke of Bavaria, 'Zeitschr. f. Biologie,' xiv, p. 51; Voit, ibid., p. 57.

Accordingly, the only point admitting of discussion is the *quantitative* importance of this regulative involuntary elevation of the heat-production with respect to the maintenance of our bodily temperature. On this subject, the opinions of the most competent writers are at variance. Pflüger is inclined to attribute a very high value to this mechanism, while Voit believes that compared with other means its importance is essentially very slight. For the rest, it is possible that this mode of regulation plays a much more important *rôle* in wild than in tame and less robust domestic animals—although the thicker fur and increased subcutaneous fat with which wild animals are provided during the cold season of the year, as well as their inclination to seek the protection of sheltered spots, clearly goes to show that in them too the regulative increase of heat-production is insufficient. A man, if obliged to rely on this latter alone, would fare still worse. For, as Senator* has shown, a naked man cannot maintain his bodily heat in an external temperature lower than about 27° C.; without clothes it would only be possible to save ourselves from a considerable reduction of bodily heat at the ordinary temperature of our rooms by very energetic muscular exertion and the consumption of large quantities of food; and if the inhabitants of arctic regions did not envelop themselves in thick skins, the regulative plus-decomposition would certainly not save them from being frozen. As for the occurrence in man of a regulation of heat-production in an opposite direction, *i. e.* a diminution independently of volition of the oxidative processes when the external temperature is high, this is considered doubtful by Voit, and at any rate he attaches still less importance to this regulation than to the involuntary increase of production in cool surroundings: and it is also apparent that even in a person who is perfectly at rest and fasting, the production of heat cannot fall below a definite point as long as he lives and breathes.

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* Senator, 'Virch. A.,' xlv, p. 351; l, p. 354; 'A. f. Anat. u. Physiol.,' 1872, p. 1.

There exist, as you perceive, a great number of very potent agencies by which both the production and loss of heat may be influenced in a regulative manner. But however excellent these means, and however well they are adapted to maintain a constant bodily temperature under the ordinary internal and external conditions—*their capacity is not unlimited;* and you need, therefore, feel no surprise should the sum of the natural and artificial regulative contrivances fail in the presence of influences which are calculated to produce enormous alterations of bodily temperature. True, during *disturbances of heat-production*, there appears to be no such failure in man. Even when in a pathological condition, the production of heat is permanently reduced to a very low standard, the body does not grow cooler, provided the skin and its vessels act normally. The temperature does not usually fall below the lowest normal values in persons who are condemned to chronic inanition owing to stricture of the œsophagus, in individuals who are deprived of the use of a great many of their muscles in consequence of a cerebral affection or who are compelled to remain at rest through any other accident, or in patients exhibiting the extremest degrees of anæmia; and if a slight decrease of bodily heat is observed to attend suffocative respiratory lesions, the cause of this is not a diminution of the oxidative processes but a disturbance of the cutaneous circulation, which we shall soon have occasion to discuss. On the other hand, a diabetic patient may consume enormous quantities of food of all kinds, but he does not therefore become warmer than a healthy person; and that any profuse glandular secretion could abnormally raise the bodily temperature, is absolutely out of the question. Energetic muscular contractions form, apparently, the sole exception to the rule. During *epileptic* and *uræmic* paroxysms, and more especially in *tetanus*, both of the traumatic and rheumatic varieties, very extreme temperatures have been recorded by numerous observers; temperatures of from 42·5° to 43° or even as much as 44° C. have been registered, and a further rise to almost 45° has occasionally been noticed after death. Here it is unquestionably a natural thought, to refer the excessive increase of heat to the intense and wide-spread muscular contractions, all the more so because scarcely any energy is converted during these tetanic contractions into mechanical effect: an oft-quoted experiment of Leyden,[*] who succeeded, by producing repeated attacks of tetanus in a dog, in raising the temperature in two hours from 39·6° to 44·8, that is by 5·2°, also appears to tell decidedly in favour of this idea. Nevertheless, it is questionable whether a disturbance of heat-regulation does not co-operate in these cases also. For while the skin in tetanus is usually warm and often enough covered with sweat, we are ignorant whether in this disease the dilatation of the cutaneous vessels is as marked as in violent voluntary muscular exertion, or whether other factors, such as a simultaneous stimulation of the vaso-motors of the skin or a diminished irritability of the inhibitory nerves, may not here intervene to disturb regulation. So much is certain at any rate,—that the most forced and persistent voluntary muscular contractions are only capable of raising the bodily temperature of a healthy man, as a rule, by but a fraction of a degree, or at most by a whole degree, and this only temporarily.[†] Calberla[‡] convinced himself that the heat of

[*] Leyden, 'Virch. A.,' xxvi, p. 538. Cf. also Heidenhain, 'Pflüg. A.' v, p. 77.

[†] Cf. Obernier, 'D. Hitzschlag, Insolation, &c.,' Bonn, 1867, p. 80; Jürgensen, 'D. Körperwärme des gesunden Menschen,' Leipsig, 1873, p. 46; Jaeger, 'Ueber d. Körperwärme des gesunden Menschen,' I.-D., Leipsig, 1881; also 'D. A. f. klin. Med.,' xxix, p. 516.

[‡] Calberla, 'A. d. Heilkd.,' xvi, p. 276.

the body remained—contrary to former statements—almost constant during several hours spent in mountain-climbing; and Voit[*] has even observed the occurrence of a fall of temperature, owing to the rapid evaporation of water, in a man working to the full extent of his powers.

On the other hand, the regulative mechanisms prove much less perfect in presence of conditions exerting a very considerable influence on the *loss of heat*. If, as you have just heard, the bodily heat of a naked man can be kept up by his natural means of regulation only in a temperature of at least 27° C.; and if consequently, when the external temperature is lower, the cooling of the body can only be averted by suitable clothing and lodging, as well as by a corresponding increase of food and muscular exertion; it is clear without further explanation that an imperfectly nourished and thinly clad individual who lies in the open air, wearied out or sleeping, in the extreme cold of winter runs an imminent risk of being frozen. Naturally, the cooling will take place more rapidly in proportion as the cutaneous vessels are dilated, and the greater, consequently, the difference between the temperature of the skin and that of the surrounding atmosphere (or ground); and in this we see one of the reasons why *e. g.* a drunken person so rapidly loses heat in cold surroundings,[†] though, it is true, such persons cannot properly use their limbs. But the cutaneous arteries may be very narrow and the entire surface of the body be extremely anæmic, yet at the low temperature of the air in winter, often considerably below 0°, the loss of heat from the skin and lungs can never, while life lasts, cease to be considerable, and the temperature of the body will therefore certainly fall, although perhaps only slowly. What then happens and how the organism reacts to the reduction of its temperature has not, for obvious reasons, been carefully observed in man; such observations, however, may be conveniently carried out on animals.[‡] With this object, one need only immerse a rabbit or a small dog up to the neck in water at about 0° for a short time; or the animal may be placed in a receptacle, surrounded by a freezing mixture and so narrow as to prevent all movement: the bodily temperature will then gradually fall to an extent which will be greater the longer the time spent in the cold medium. If the animal be removed after its rectal temperature has fallen to 18° or 20°, it cannot support itself on its legs, but lies motionless on its side; the number of heart-contractions is now very small, scarcely sixteen to twenty beats in a minute; the frequency of the respirations is also greatly diminished, or the breathing is rapid but extremely superficial; the smooth musculature of the intestines and urinary bladder behave as if paralysed, the peristaltic movements are completely arrested, and the bladder, even when very full, is never evacuated. The eyes remain wide open, and on touching the cornea, winking, if it occurs at all, takes place very slowly; the pupils are also very dilated, and, as a rule, either do not react to light or respond very tardily. In short, the animals exhibit *a kind of general paralytic condition*, which undoubtedly depends on very reduced irritability of all the tissues, and in particular of the nervous system. If the animals cooled to 18° be allowed to remain longer in the cold medium, death as a rule takes place rapidly, and frequently with convulsions; yet, as Horvath has shown, the cooling may be pushed much further, if artificial respiration is at the same time maintained. What reduction of bodily temperature is fatal to man we do not know, and we are also ignorant as to whether convulsions appear immediately before the end; we find post mortem, as might be anticipated, anæmia of the peripheral and hyperæmia of the internal parts, together with pulmonary œdema, if the left ventricle had been paralysed earlier than the right: this latter appearance, however, is comparatively rare, since in most cases of death by extreme cold the fatal result is due to general paralysis of the heart. But even the animals removed from the cold medium when their temperature has fallen to 18° do not usually recover on being allowed to lie quietly exposed to the ordinary heat of the room. They may remain for many hours in their paralytic condition without any further cooling taking place, but by degrees the heart-beats and respirations become steadily feebler till they finally cease. On the other hand, the animals cooled to 18° can be restored to their normal bodily temperature on being transferred to a warm medium: in a receptacle at 40°, Walther required from two to three hours in order to raise the temperature from 18° to 39°, and he found that the bodily warmth first increased very slowly but afterwards very rapidly as soon as 30° had been reached. It is still more interesting to find that this restoration of heat can also be accomplished by means of artificial respiration. The air introduced during the process does not act by directly warming the animal; for the restoration of heat also follows when the inspired air is several degrees lower than the bodily temperature of the cooled animal. The restoration is due to the heat-production of the animal body, and the artificial respiration is simply the means of securing that the irritability of the various centres shall not be destroyed before the oxidative processes have been properly set going. Moreover, this restoration of heat by artificial respiration takes place with extreme slowness, so that ten times as long a period is needed for it as would be required were the animal placed in a medium the temperature of which is high. The process of heat-production is here the same as that by means of which a less markedly cooled animal recovers without artificial respiration, though then also a long time is needed for restoration. As the bodily temperature is raised by warming the animal, the power of motion and the energy of the smooth muscles are gradually recovered, urine is passed, and the evacuation of fæces testifies to the recommencement of the peristaltic movements; the respirations become deeper, the heart-beats more frequent, and the blood-pressure rises. The sensorium is the last to be restored: the rabbits usually fall asleep when warmed to about 30°, and do not behave like healthy, active animals till the normal temperature is established. As to the lowest degrees of body heat that have been survived in man, I can give you no information. Temperatures of 30° to 26° or even 24° have repeatedly been registered in the rectum,* mostly in drunken, ragged vagrants, picked up off the streets in winter; and, like the animals experimented upon, these persons also exhibited marked apathy and somnolence, while at the same time the pupils were dilated and sluggish, and the pulse and respirations infrequent. In these cases also, several hours usually elapsed before the affected individuals, though wrapped in warm blankets, regained their normal temperature; with the rise of bodily warmth, the number of heart-beats and respirations increased, the deep sleep gradually became lighter, till at last full consciousness returned. No subsequent disturbance of the general state ensued in favorable cases. Still, you will not look upon such a transitory reduction of temperature as an insignificant occurrence. For the nearer the fall approaches values of from 18° to 20°, the more doubtful is a complete and rapid restoration. Many of the cooled animals die even after they have regained their normal warmth; in many others, the rise of temperature does not stop at the normal elevation, but mounts more or less, perhaps several degrees, above it, and the animals in whom this happens usually become extremely emaciated during the next few days, so that they only very slowly regain strength or never do so. In man also, such elevations of temperature have often been determined after transitory cooling, thus affording evidence that the equilibrium between production and loss of heat has been persistently disturbed by the powerful agency of cold.

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[*] Voit, 'Zeitschr. f. Biol.,' xiv, p. 156.

[†] Reincke, 'Deutsch. A. f. klin. Med.,' xvi, p. 12; Weiland, 'Drei Fälle von niedrigen Körpertemperaturen,' Inaug.-Dissert., Kiel, 1869; Peter, 'Gaz. hebdom. d. Paris,' 1872, Nos. 31 and 32.

[‡] Walther, 'Virch. A.,' xxv, p. 414; 'Med. Centralb.,' 1864, p. 801, 'A. f. Anat. und Physiolg.,' 1865, p. 25; Horvath, 'Pflüg. A.,' xii, p. 278.

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* Reincke, 'Deutsch. A. f. klin. Med.,' xvi, p. 12; Weiland, 'Drei Fälle von niedrigen Körpertemperaturen,' Inaug.-Dissert., Kiel, 1869; Peter, 'Gaz. hebdom. d. Paris,' 1872, Nos. 31 and 32.

Prolonged exposure to *an abnormally warm* external temperature must have an exactly opposite effect on the heat of the body. The warmer the surrounding air, the less will be the quantity of heat lost by radiation and conduction; and since our organism continually produces considerable amounts of heat, even though to the voluntary decrease of production there is added an involuntary one, the inevitable result must be a rapid disturbance of equilibrium with a tendency to *overheating*. If, nevertheless, a man can maintain his bodily heat at the normal standard in external temperatures differing little from that of the body itself, this is mainly owing, as you know, to the profuse secretion of sweat which sets in under these circumstances, and to the considerable loss of heat which attends the evaporation of the sweat; so rapid is the evaporation in a dry atmosphere that the body can even withstand for a time a degree of heat considerably in excess of its own, without experiencing any increase of temperature. Yet this also has its limits; and on exposure for a time to dry air of from 50° to 60°, even the most profuse sweating cannot save the body from overheating. The danger is still greater in this respect when the rapid evaporation of the sweat or expired water is rendered difficult or prevented by the overloading or even saturation of the air with moisture, for here a lower external temperature will suffice to give rise to considerable overheating. This fact has repeatedly been verified on men in the vapour-bath; but more exact observations are only feasible here also by experiments on animals.* The method to be adopted is very simple. The animals are placed in a chamber with double walls, the space between which is filled with water that may be raised to the desired temperature by means of a regulated gas- or spirit-flame; in the case of the animals usually experimented upon, such as rabbits, dogs and guinea-pigs, with their imperfectly developed and inactive sweat-glands, it matters little whether the air of the chamber be dry or saturated with moisture. Rosenthal, experimenting on rabbits, which were allowed to sit free without restraint, convinced himself that these animals can maintain their bodily heat unaltered in air of from 11° to 32°, but that their temperature rises when the air of the chamber exceeds 32°. There is an increase to 41°—42° when the atmosphere is warmed to 36°; and at this elevation a state of equilibrium is established and may persist for a long time. Perfectly harmonious results were obtained in my institute on guinea-pigs, whose temperature rose to 41°—42° in air at from 36° to 37°, and remained for days at this elevation.† After a short period of extreme restlessness, the animals lie sprawling on the belly with their legs widely separated, in order to present as great a surface as possible to the surrounding medium; respiration is greatly accelerated and very superficial, the heart-beats can scarcely be counted, the skin is throughout very hot to

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* Obernier, loc. cit.; Rosenthal, loc. cit., 'Handb.,' p. 335; Bernard, 'Vorlesungen über thier. Wärme.,' Uebers. von Schuster, Leipsig, 1875, p. 325, *et seq.*

† Litten, 'Virch. A.,' lxx, p. 10.

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the touch, and where, as in the ears, the vessels can be directly observed, they are evidently greatly dilated. All these phenomena become still more conspicuous when the temperature of the chamber is raised above the values stated to close on 40°. As the air becomes heated, the temperature of the animal rapidly rises, and when, on exposure to 40°, it has reached 44°—45°, the respirations are enormously accelerated, the pulse is almost fluttering and cannot be counted, the pupils are dilated, all the cutaneous vessels are extremely wide, and the animal lies there with perfectly relaxed muscles in an almost paralytic condition. The most extreme caution is now imperative. For after long exposure to such hot air, death very easily occurs, and is very often preceded by more or less wide-spread muscular twitchings and convulsions, especially when the heating has rapidly taken place. If the temperature now be raised still further, death is inevitable. For it is a universal law that animal life is incompatible with bodily temperatures which exceed a certain elevation. The limit in warm-blooded animals is about 5°—6° above the normal mean temperature; if the bodily heat exceeds this, animals and men perish without exception. The cause of death is not, as has been supposed, a rapid coagulation of the blood, nor is it a heat-rigor of the muscles, since this only sets in at 48°—50°; it is the exhaustion and paralysis of the nervous and contractile apparatus, and in particular a complete *paralysis of the heart* that destroys life. When the temperature has been artificially raised to more than 42°—44°, the arterial pressure, which was previously high, falls rapidly (cf. vol. i, p. 91); and if the animal's thorax be opened immediately after death the heart will be found arrested in diastole; the right side is, as a rule, greatly overfilled, and mechanical or electrical stimuli excite no proper contractions, while irritation of the phrenic is not responded to by a contraction of the diaphragm. For the rest, the occurrence of abnormal chemical processes in the tissues of the body as the result of the overheating is indicated by the facts that the blood, which of course is very dark, rapidly coagulates post mortem while rigor mortis sets in very early. Yet we have still more convincing evidence of this in the conspicuous alterations undergone by the metabolism of the animals as the result of the retention of heat. Naunyn* first determined that a dog, whose rectal temperature has been raised in an overheated space from 35° to 42·5°, produces on the same day a very considerably *increased amount of urea*. On the other hand, Erler and Litten found, as I have already told you (vol. ii, p. 671), that animals whose temperature is raised by the retention of heat may in individual instances experience a *reduction* of the *carbonic acid excretion* by as much as 50 per cent., a change which is undoubtedly associated with a diminished absorption of oxygen. Moreover, I also mentioned on that occasion that we had observed extensive fatty changes in the liver, heart, kidneys, and voluntary muscles, under the influence of the simultaneous increase of the albuminous waste—as evidenced by the augmented production of urea—and of the diminution of the oxygen-supply. Lastly, that the loss of water experienced by the animals in the warm chamber amounts to several times the normal, in spite of the imperfectly developed sweat-glands, is proved by the reductions of weight apparent on repeated weighing; the decrease also becomes sufficiently manifest through the striking and rapid emaciation of animals which have spent several successive days in air at 36°—37°.

It is not to be wondered at that, under these circumstances, a heating due to retention of warmth, even when not pushed to a fatal issue, should be attended by various evil or indeed actually destructive effects. Thus, our guinea-pigs all died when kept long in the warm chamber, even when their bodily temperature had never exceeded 42°, the longest period survived by them being five to six days. Even when the animals were removed after passing some days in the chamber, they could not always be kept alive. Their temperature soon falls when restored to the ordinary heat of the room, and this whether the overheating had been brief or prolonged; but the fall is not uncommonly below normal, more especially after protracted rise of temperature. This is readily explainable by the fact that the paralysis of the cutaneous vessels under the influence of the excessive heat persists after the animal is removed. The great loss of heat necessarily attending the dilatation of the vessels of the skin causes a fall of bodily temperature; if the reduction does not exceed a few degrees the animals recover after a time; but if the rectal temperature is still further reduced, recovery becomes doubtful: the animals then remain feeble and apathetic, do not eat properly, most likely get diarrhœa, and finally die, without developing any new or striking symptoms. An especially noteworthy fact has been discovered by Rosenthal, however,—that an animal which, after being overheated, regains or almost regains its normal temperature, when again placed in the hot medium, behaves differently from the first occasion. *The rise of temperature is much less extensive* than formerly; hence the respiration and pulse are not so accelerated, the musculature is not so relaxed; in short, the whole condition of the animal is not so threatening. The longer the time elapsing between the first and second experiments, the less distinct is the difference in the effects; on the other hand, this difference may be still further increased on several repetitions of the experiment. The higher the temperature to which the animal has been subjected, the better will it resist subsequent exposure to heat, yet even a stay in air at about 32° may afford a certain amount of protection against the occurrence of serious overheating when the animal is afterwards exposed in a still warmer medium. The factor on which the habituation of the organism to prolonged exposure to high temperatures depends has not as yet been fully explained. It is not an augmented loss of water; for the difference between habituated and non-habituated animals is precisely the same, even when the warm air of the hot chamber is saturated with moisture; indeed, the loss of water on remaining in warm air is much slighter in habituated than in non-habituated animals. Nor does it appear in what other way this habituation could be connected with loss of heat, and accordingly we have scarcely any alternative but to assume that the production of heat is diminished in these emaciated animals, which shortly before were so seriously affected. True, we are not yet, so far as I know, in possession of investigations into the metabolism of the habituated animals.

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* Naunyn, 'A. f. Anat. u. Physiolg.,' 1870, p. 159.

That in man also the bodily temperature is raised by remaining in a hot medium is not only to be inferred theoretically, but has, as already indicated, been repeatedly observed. Schleich,[*] for example, found that on remaining for one hour in a bath, the water in which was raised to 40°—41°, the temperature of his mouth had increased to 39·5°, 39·6°, or even 39·9°. In Krishaber,[†] the temperature of the axilla rose from 36·6° to 39·6° on exposure for twenty-six minutes to dry air at 60°—70°, and on remaining in a vapour-bath at 40°—45° it increased in forty minutes to as much as 40·2°.[‡] Moreover, the known results of increase of temperature due to heat-retention also set in. The individual grows restless and uncomfortable, respiration becomes very frequent, and the number of heart-beats increases enormously —from 73 to 160, 180 or still more. Further, the augmented production of *urea* under these circumstances had formerly been established by Bartels, and was then investigated with great accuracy by Schleich, as well as by Frey and Heiligenthal;[‡] the latter also found an increase in the excretion of *uric acid.* Finally, Krishaber also states that his body became habituated to the high temperatures on repeating the hot air or vapour baths. Such being the position of affairs, you can have no doubt that an excessive rise of temperature due to heat-retention must prove just as destructive to men as to the animals experimented upon. As a matter of fact, in my opinion, every year sees the sacrifice of some individuals to abnormal rise of temperature depending on heat-retention, chiefly it is true in hot climates, but with us also during midsummer. I refer to cases of *sunstroke* or *insolation.* I willingly admit that the pathology of insolation is not sufficiently elucidated in all its aspects, yet there can be no doubt that *overheating of the body plays a decisive part*

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[*] Schleich, 'A. f. experim. Patholg.,' iv, p. 82. Similar facts were observed by Walton and Witherle, 'Boston Med. and Surg. Journ.,' vol. cii, No. 24, June 10th, 1880.

[†] Krishaber, 'Gaz. méd. de Paris,' 1877, No. 46.

[‡] Bartels (Ziemssen's 'Handb.,' ix, 1, 197) also saw the rectal temperature of a man rise by 3·6° on exposure for thirty minutes in a vapour-bath at 53°. Cf. also Burkhardt, 'D. med. Wochenschr.,' 1881, No. 21; Frey und Heiligenthal, 'D. heissen Luft- u. Dampf-bäder in Baden-Baden,' Leipsig, 1881; further, the very interesting statements as to the influence of working in St. Gothard's tunnel on the bodily temperature, by Stapff, 'A. f. Physiol.,' 18 [illegible].

in it. In the first place, very excessive temperatures have been repeatedly registered in individuals attacked by sunstroke; thus Bäumler[*] records 42·9° in a fatal case one hour after admission to hospital, and much higher temperatures have been found by American physicians.[†] Even though, for obvious reasons, exact measurements have not been made in the great majority of cases of sunstroke, the enormous heat of the face and entire skin usually attracts the notice even of the laity. In the next place, the symptoms of insolation agree very closely with those of the overheated animals; the face is red, the respiration hurried and gasping, the pulse enormously retarded, the pupils dilated; the patient is unconscious and delirious, and the fatal collapse is often preceded by convulsions. The last is especially the case when the affection arises very rapidly; when its development is more protracted and gradual, the signs of collapse early become prominent. Nor is there any difficulty, so far as I see, in explaining the overheating of the body in sunstroke. The persons usually attacked are almost always those who undergo excessive muscular exertion during great heat,—with us, chiefly soldiers after long marches; and experience shows that the danger is enhanced if the atmosphere is saturated with moisture, more especially if it is *still*. This means simply that heat-production is extremely increased, while the loss of heat by conduction to the surrounding medium and by evaporation is essentially checked and restricted. Whether marching in close columns forms an additional element of danger, I shall not undertake to decide; more importance certainly attaches to the absence of free sweating in such a position. This, however, is only too often observed. Persons working in great heat usually secrete enormous quantities of sweat for a considerable time; then comes a moment when its production begins to fail, whether owing to exhaustion of the sweat-nerves or because the water-contents of the blood have been reduced by the profuse secretion. That the latter is probably the determining factor may be inferred from the very decided increase of danger which follows abstention from water: have we not lately come to recognise a regular supply of water during work as the surest means of averting the dreaded accident? So soon as the production of sweat begins to fail, and the loss of heat through evaporation ceases or is considerably reduced, there is henceforward a possibility that the heat-equilibrium may be disturbed, and that, as the result of the retention of heat, there may occur a slow or rapid abnormal, or even fatal, elevation of the bodily temperature.

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[*] Bäumler, 'Med. Times and Gaz.,' Aug. 1st, 1868.

[†] Vide Wunderlich, 'D. Verhalten d. Eigenwärme in Krankheiten,' Aufl., Leipzig, 1870, p. 134.

The deviations from the average bodily temperature hitherto discussed were essentially called forth by the action of conditions which were too abnormal in their nature to admit of compensation by the regulative mechanisms of the organism. Such extreme agencies are, in fact, absolutely necessary to the alteration of the bodily temperature, so long as the regulative mechanisms perform their office with promptness and regularity; yet it is obvious that even under ordinary conditions, a constancy of the bodily temperature cannot be counted on if these *mechanisms act irregularly* and with too little energy. In seeking to correctly estimate the significance of these errors of regulation as regards the heat of the body, it will evidently be necessary to consider the disturbances of the regulation of heat-production and those of loss of heat independently. True, it is only the disturbances of the latter category that excite considerable interest in pathology. For as regards the errors in the regulation of heat-production, perhaps the only fact of importance is the possibility that during a stay in a cold medium the voluntary and involuntary means of production may not be so efficient as in health. This is undoubtedly the case in starving persons, and to a still greater degree in those, most of whose muscles are paralysed or otherwise withdrawn from the control of the will. The heat-equilibrium of such individuals is really less stable than that of healthy persons. That their bodily temperature does not, it is true, depend, as in the poicilothermal animals, on the temperature of the surrounding medium is assured while they live and breathe, and so long as the cutaneous vessels and the blood-stream through them obey physiological laws; still it is unquestionable that curarised animals become cooled relatively rapidly in a cold medium, and that starving and paralysed individuals are much more exposed during the severe cold of winter to the danger of being frozen than are well-nourished persons with healthy muscles. Nevertheless, the muscular paralysis must be very extensive, if the constancy of the bodily heat is to be seriously threatened, even under unfavorable conditions of external temperature. I should have refrained from mentioning this, as being self-evident, had not Samuel* recently asserted that the bodily heat of the rabbit becomes, as he expresses it, "the sport of the external temperature," when both the subclavians and femoral arteries are ligatured, or both cervical plexuses together with the sciatic and crural nerves are divided. He has become convinced of this in consequence of a series of experiments, in which he states he has found that while vigorous rabbits suffer no diminution of bodily heat even after twenty-four hours' exposure in air at about 0°, equally large animals in whom the muscles of the extremities have been rendered inactive in the manner described undergo a continuous cooling in from four to eight hours to 22°—20°, and perish with the signs of death from extreme cold. A number of other experiments by Samuel, in which he produced various injuries of the abdomen in rabbits and sought to determine the share taken by the injured organ in the production of heat, by systematically recording the temperature of the animals after operation, have probably seemed too ambiguous to his critics to be received with continued respect; the experiments on the extremities, however, are described with such precision by their originator that they are quoted by the most cautious writers as well accredited. And yet two things must equally cause us to hesitate before accepting Samuel's results—the circumstance that the ligature of the arteries just mentioned does not completely deprive the rabbit's extremities of motion, and the slight bulk of the extremities relatively to the entire body of the animal. On a repetition of these experiments in my institute in Breslau, our results were very far from being in conformity to Samuel's statements. Some of the animals with ligatured arteries or divided nerves perished, it is true, within 12—24 hours after being placed in an ice-chest of moderate size, the temperature of which remained at about 0°; others, however, which were similarly treated continued for several days in the ice-chest without any injury to health, and in particular without any noteworthy reduction of bodily heat. But perfectly sound animals behaved in the same identical fashion, some dying and others remaining perfectly well. Nevertheless, it does not occur to me to question Samuel's results. I dispute simply that his rabbits died in consequence of the cooling; on the contrary, as I gather from his description, *the temperature of his animals fell because of the near approach of death.* But the regularity with which Samuel's animals perished would certainly be a wonderful mishap if the animals were really healthy. I cannot help suspecting that diseased animals were repeatedly employed. I infer this more particularly from his repeated statements as to the presence of *pneumonia,* which was often found post mortem and is described as "violent" or "strong;" and this too in rabbits which had only survived the commencement of the experiment by eleven, nine, or even three hours.* Certainly, no one but Samuel himself will be inclined to attribute the production of such violent pneumonia to so short an experiment.

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* Samuel, 'Ueber d. Entstehung d. Eigenwärme u. d. Fiebers, Leipsig, 1876.

In its power of influencing the temperature of the body, much greater importance attaches to *disturbance of the mechanism controlling the loss of heat.* For while disturbances of the regulation of production only prove prejudicial when unusual conditions influence the loss of heat, an abnormal behaviour of the apparatus by which heat is yielded up may very seriously interfere with the constancy of the bodily temperature under conditions which are in other respects perfectly normal. The decisive factor in maintaining a constant temperature is, as you already know, *the state of the blood-stream through the cutaneous vessels.* The narrowness and anæmia of the arteries of the skin when the heat-production is slight and the temperature of the surrounding medium low, and, on the other hand, their dilatation and ample blood-supply during abundant heat-production and in warm surroundings, are the most effective means at the command of the organism for the maintenance of its temperature constant. Compared with these, the action of the sweat-glands is of secondary importance; and may here be the more freely neglected, since, provided the sweat-centres are normal, the rule is for the secretion to coincide with the congestive vascular hyperæmia and the secretory pause with the anæmia, so that both tell in the same direction. If, accordingly, the alterations in the circulation of the cutaneous vessels are really to promote the constancy of the temperature, neither their contraction nor dilatation must be interfered with or prevented at the proper moment; and if, owing to any factor, the tone of the cutaneous arteries is permanently reduced below the normal, this obviously means that the organism is deprived of its best aid in protecting itself against cooling under unfavorable circumstances also. In this respect the state in which we ordinarily live is unfavorable, *i. e.* existence at the usual temperature of our rooms or at the average temperature of our temperate zone, excepting of course the days of midsummer—to say nothing of the unfavorable conditions presented by the air of winter. The causes of pathological congestive hyperæmias in a vascular area are known to you from our discussion of the local circulatory disturbances, and no other cause is found in connection with the skin. More or less extensive cutaneous hyperæmias may occur on a *nervous* basis, *e. g.* as an associated symptom of neuroses, and may depend either on irritation of the inhibitory nerves or on paralysis of the vaso-motors. The physiological analogue of the first form is the dilatation of the cutaneous vessels which ensues on irritation of the sensory nerves or occurs during asphyxia; that of the second is the hyperæmia of the vessels of the ear after division of the cervical sympathetic in the rabbit. That on irritation of the sensory nerves as well as during asphyxia, the temperature of the blood does actually undergo a slight fall, we have learned from Heidenhain's* well-known experiments; and it was long since shown in Donders'† laboratory that bilateral section of the cervical sympathetic may for a time reduce the bodily heat of a rabbit by 2°, the normal elevation being regained only when the dilatation of the vessels of the ear has begun to recede. Whether subnormal temperatures have also been registered in men with such angio-neuroses, I am not aware, yet if the reduction fails to set in in these cases, it can only be because of the small size of the hyperæmic cutaneous area. The more extensive this area, the more certain, naturally, is the lowering of temperature. When a dog secured upon its back cools more easily and more markedly in the curare- or morphia-narcosis than it otherwise would, it is because the greater extent of free surface is promotive of it, while to this is added a more or less pronounced dilatation of the cutaneous vessels. That drunken persons suffer a more rapid and marked cooling of their bodies than sober individuals, on exposure to cold air, I have recently stated.

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* Samuel, loc. cit., pp. 40, 39, 36.

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* Heidenhain, 'Pflüg. A.,' iii, p. 504.

† Cf. the abstract in Henle u. Meissner's 'Jahresber.' for 1866, p. 368.

In the next place, hyperæmias of the skin occur which do not depend upon nervous agency, but on the direct action of some factor on the cutaneous arteries. To this category belongs the paralysis of these vessels which results from very high temperatures of the medium surrounding the skin; with regard to which I have already stated that it may persist for a considerable time after the return of the individual to cooler surroundings, more especially if the action of the heat had been prolonged and very intense: the consequence under certain circumstances is a very considerable reduction of bodily heat. The fluxion to the cutaneous vessels and the resulting loss of temperature is still more considerable in rabbits *which have been coated with a varnish impervious to perspiration.* The marked dilatation of the cutaneous vessels beneath the coating of varnish has long attracted attention at the autopsy of the animals thus treated, and during life can best be demonstrated by partial application of the varnish, for so far as the coating extends the temperature in and under the skin is considerably higher than that of uncoated spots. Moreover, the increased loss of heat from the varnished skin has been directly demonstrated by Rosenthal and Laschkewitsch* by calorimetric means. When the entire superficies is covered, the loss of heat becomes so considerable in the rabbit that its temperature gradually falls to a degree no longer compatible with life: small animals with a relatively large surface die earlier than larger specimens. That the cooling alone is the cause of death in the varnished rabbits is proved by the fact that when it is prevented the fatal termination is also averted. When the animals are at once packed after varnishing in thick wadding, they do not die, nor do they present any abnormal appearances if the external temperature be high.* For the rest, you will carefully note that all this applies only to rabbits, and perhaps also to a few other animals with equally thin and delicate skins; the occurrence of the much-discussed and greatly dreaded "suppression of cutaneous perspiration" is not for all animals a dangerous or fatal event. No practical inconvenience is produced in dogs by coating with varnish, tar, linseed oil, collodion, &c., nor does any reduction of temperature worth mentioning occur in them; and in man also it appears, according to some experiments by Senator,† that the varnishing has no effect on the bodily heat, probably because, as already hinted at, the thickness of the skin guards against such energetic paralysing action on the arteries passing to it.

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* Laschkewitsch, 'A. f. Anat. und Physiol.,' 1868, p. 61.

Moreover, the fall of temperature, which, as a rule, follows *extensive scalding* of the skin, is certainly due to the abnormally increased loss of heat, within the scalded parts, from the vessels which are dilated and deprived of their protective covering of epidermis.‡ True, that the cooling brings about the death of the injured persons is quite out of the question; were this the case nothing could be simpler than to guard against the loss of heat, and thus to avert the fatal course which, as you know, the physician's art is at present powerless to prevent. The fall of temperature plays only a subordinate *rôle* as compared with the other severe lesions accompanying extensive scalding, in particular the deleterious action on the blood which mainly proves fatal in such cases.

In traumatic *solutions of continuity of the spinal cord,* and in other diseases by which its conduction is interrupted, there is also no dearth of various other severe functional disturbances; yet alterations of bodily temperature form a frequent and important feature of these affections. This is easily understood. For all the arteries whose vaso-motors leave the cord below the interruption are deprived of their tonus for a time, and although this may ultimately be recovered, a certain period must first elapse during which the vessels are dilated and consequently overfilled with blood. Now, here the conditions are, it is true, somewhat complicated, firstly, because the vaso-motor innervation is in abeyance not only in the case of the arteries on which the loss of heat depends, *i. e.* chiefly the cutaneous arteries, but also in the case of those supplying the organs engaged in heat-production; and, secondly, because the effects of a solution of continuity of the cord differ greatly according to the level of the interruption. The lower the situation of the latter, the less liable is the arterial pressure to suffer, while high interruptions are always followed by a considerable fall of arterial pressure and hence by retardation of the blood-stream. The crucial point in rabbits and the herbivores generally is the situation of the interruption *above* or *below* the exit of the splanchnics, which in dogs, as is well known, have not such far-reaching importance for the blood-pressure. The effect of the circulatory disturbance in question on the loss of heat can be more accurately stated than can its influence on heat-production. That the production is diminished by a general slowing of the circulation is not, I think, open to doubt, but we are ignorant whether a neuroparalytic congestive hyperæmia increases the production or leaves it unaltered. It is perfectly certain, on the other hand, that a hyperæmia of the cutaneous vessels accompanied by an acceleration of the blood-stream, *i. e.* congestion with the blood-pressure unaffected, increases *cæteris paribus* the loss of heat, while a retardation of the blood-stream through the vessels of the skin will necessarily diminish the loss. If you consider in addition the, if you will, indirect influence which attends a solution of continuity of the spinal cord, in consequence of the other consecutive disturbances, in particular the cessation of voluntary movements, you will feel no surprise that the effect of the interruption on the temperature of the body should in different cases prove very dissimilar.

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* Valentin, 'A. f. phys. Heilk.,' 1858, p. 433.

† Senator, 'Virch. A.,' lxx, p. 182.

‡ Cf. Falk, 'Virch. A.,' liii, p. 27.

As a rule, crushing, laceration, or cutting through of the spinal cord is immediately followed by a not inconsiderable *fall* of bodily temperature, which must be attributed no doubt to the paralysis of the cutaneous vessels and the consequent increase in the loss of heat. In a number of cases, especially of solutions of continuity, the heat of the body is rapidly *restored to the normal* standard, at which it henceforth remains; here the cutaneous arteries have recovered their tone; and that the paralysis of the lower extremities does not so greatly diminish the heat-production as to jeopardise the heat-equilibrium, you already know. In a second series of cases, on the contrary, *the fall of temperature is persistent;* indeed, it goes on gradually increasing, so that the affected individuals are slowly or rapidly cooled to a degree which endangers life, and they perish with all the signs of death from extreme reduction of temperature. It is not to be denied that the diminished heat-production is partly responsible for this result, especially in very protracted cases; yet the fact that the cooling may be considerably delayed by enveloping the patient in badly conducting materials or by raising the surrounding temperature proves how great a part is played by increased loss of heat. Much greater interest is excited, however, by those cases in which the primary reduction of bodily heat is *followed,* after a few hours, by an abnormal rise of temperature, a rise to the very highest values ever found in man or mammals, of 43° or even 44°. Such excessive temperatures have repeatedly been registered in men after compression and laceration of the cervical cord;[*] and they have also been observed in rabbits and dogs on experimentally injuring the upper sections of the central nervous system. The earliest statements on this subject are contained in a paper by Tscheschichin,[†] for which, however, Rosenthal, under whose supervision the research was carried out, declines all responsibility; this investigation goes to show that separation of the medulla oblongata from the pons is followed by a considerable rise of temperature. Naunyn and Quincke* subsequently studied this question with great care, and have come to the conclusion that laceration of the cervical cord in dogs causes a very considerable increase of bodily heat, when loss of heat is prevented by placing the animals in a hot chamber at a temperature of 26°—30°,—a temperature, that is, which would be insufficient to cause an abnormal increase in uninjured dogs; they also found that in very large dogs, at least at summer-heat, the mere envelopment in badly conducting materials is enough to cause a *slight* elevation of temperature. Moreover, it was found by Wood,† in an extensive series of experiments, that a cut through or below the medulla oblongata lowers, as a rule, the bodily heat; on the other hand, he observed, not it is true in rabbits, but in dogs, a considerable rise of temperature on dividing the medulla from the pons, thus confirming Tscheschichin's observations. Heidenhain‡ also occasionally obtained results similar to those of Tscheschichin, but believes that a separation of the medulla from the pons is unnecessary, a simple puncture with a fine lancet-shaped needle in the region of the posterior border of the pons and anterior border of the medulla sufficing to raise the bodily heat by several degrees. Similar results were obtained by Schreiber.§ Still these experiments have not escaped contradiction. Neither Rosenthal|| nor Lewitzky¶ has ever found anything but a fall of temperature on dividing the spinal cord; and on repeating the experiments just described, Riegel** and Schroff†† failed to observe a rise of bodily heat in the manner stated. Yet we cannot from this contradiction come to any conclusion except that we are still ignorant of some of the conditions which must be present when a rise of temperature

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[*] Brodie, 'Med.-Chir. Transact.,' 1837, p. 412; Billroth, 'Beobactungsstudien über Wundfieber, &c.,' 1862, p. 158; Fischer, 'Med. Centralbl.,' 1869, p. 259; Quincke, 'Berl. klin. Wochenschr.,' 1869, p. 29; Nieden, ibid., 78, No. 50.

Tscheschichin, 'A. f. Anat. und Physiolog.,' 1866, p. 151.

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* Naunyn und Quincke, ibid., 1869, pp. 174, 521.

† H. C. Wood, 'Fever; a Study in Morbid and Normal Physiology,' Washington, 1880 (Smithsonian Contributions), p. 26, *et seq.*

‡ Heidenhain, 'Pflüg. A.,' iii, p. 578.

§ Schreiber, ibid., viii, p. 576.

|| Cf. Rosenthal, 'Zur Kenntniss d. Wärmeregulirung b. d. warmblutigen Thieren,' Erlangen, 1872, p. 3, *et seq.*; further, in Hermann's 'Hdb. d. Physiolog.,' iv, 2, p. 381.

¶ Lewitzky, 'Virch. A.,' lxvii, p. 357.

** Riegel, 'Pflüg. A.,' v, p. 629.

†† Schroff, 'Wien. akad. Sitzungsber.,' März, 1876.

follows injuries of the central nervous system; and certainly the facts themselves are better established than is their explanation.

Is the rise of temperature—so runs the first question—the result of the disconnection of certain nerves from their centres, or is it due to the irritation of these nerves; is it, in other words, a *paralytic or an irritative effect?* Tscheschichin, Wood, as well as Naunyn and Quincke argue for the first, and Heidenhain for the second alternative; and if you consider how slight is the punctured wound, and further that the rise of temperature soon passes off after its infliction but may again be produced by a second puncture, it must be admitted that Heidenhain's interpretation is a very attractive one. Moreover, in the experiments of Naunyn and Quincke, the increase of temperature never appeared so late as to exclude the possibility that the action was irritative. On the other hand, it is still less questionable that compression of the cervical cord and severance of the connection between pons and medulla oblongata involve a paralysis of innumerable nerves, so that the authors so often named are quite justified in holding their opinion. And the assumption even that the paralysis as well as also the irritation of certain nervous tracts may be involved in raising the temperature will hardly appear to you too daring, on remembering, for example, that the same dilatation of the cutaneous vessels can be produced by stimulation of the dilators as by paralysis of the constrictors. As regards the possible influence of these disturbances of innervation upon the factors which determine the height of the bodily temperature, all the observers who have seen the increase of bodily heat in their experiments, conclude therefrom that heat-production is considerably augmented as the result of injury of the central nervous system: the writers adopting the theory of paralysis ascribe this to the division of fibres exerting an inhibitory influence on heat-production; while Heidenhain, on the contrary, assumes the occurrence of a direct *stimulation* of the parts engaged in the production of heat. That an increase of heat-production actually takes place in the animals is inferred from the fact that the loss of heat is not only not diminished but even increased. After inflicting the punctured wound, Heidenhain observed a rise of temperature not merely in the rectum but also beneath the skin of the inguinal region; Naunyn and Quincke also found in their animals no noteworthy differences between the temperatures of the rectum, the hollow of the groin, and the external auditory meatus; and because, in their opinion, the dilatation of the cutaneous vessels, following compression of the cervical cord, always considerably augments the loss of heat, so much so even as to over-compensate the increased production, they wrapped the larger animals in warm coverings and placed the small ones, with a relatively large superficies, in a hot chamber. Here, however, their argument appears to me to present some flaws. For that the bodily heat of an animal will *cæteris paribus* be more increased in a warm than in a cold medium is not particularly remarkable, and affords no evidence that in the absence of external warmth the yield of heat would be increased in excess of the normal standard. Moreover, from dilatation of the cutaneous vessels we cannot, you are aware, infer an increased loss of heat, unless it be at the same time determined that the blood-pressure continues unaltered; and if, while the temperature of the internal parts is high, the subcutaneous cellular tissue and the skin itself are warm, this also does not admit of any sufficient conclusion as to the occurrence of an excessive and disproportional loss of heat. There is as yet a dearth of adequate calorimetric experiments on these animals, so that we cannot regard the loss of heat as a certainly established factor, or accurately estimate its amount. Now, it is true that Wood* has detected calorimetrically a moderately increased loss of heat in dogs in which he had carried out the high division of the cord; but against this we have the experiments of Pflüger† on the metabolism of these animals telling directly against any augmentation of the heat-producing processes. For in rabbits whose cord he had divided at the level of the seventh cervical vertebra, he found not simply no increase but even *a very marked diminution of oxygen consumption and carbonic acid elimination*, and sometimes indeed a reduction of the metabolism to half the normal values. Would it not be proper under these circumstances to give the most prominent place, or at any rate to attach considerable importance, to the *retardation of the circulation* and *feebleness of the respiration* in these animals, severely injured as they are? Both these factors reduce the loss of heat from the skin and lungs, and are thus well adapted, even in the absence of a simultaneous increase of heat-production, to raise the bodily temperature.

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* H. C. Wood, 'Fever; a Study in Morbid and Normal Physiology,' Washington, 1880 (Smithsonian Contributions), p. 26, *et seq.*

† Pflüger, his 'Archiv,' xii, p. 282; xviii, p. 247.

This, so far as I can judge, is the present state of this interesting controversy, a state which cannot be said to be very satisfactory. But if a comparatively simple experiment, which at any rate admits of an exact statement of the problem, is still attended by so much doubt and uncertainty, you cannot be astonished that we should so far also be unable to give a satisfactory explanation of certain excessive temperatures which are observed in diseases of the nervous system. Wunderlich* in Germany first directed attention to the fact that, in a great variety of diseases of the central nervous system, the bodily heat may towards the end rise gradually or rapidly to very considerable values, reaching 42° or even 43° and 44°, and has called this elevation of temperature the *agonal* or *preagonal*. Since then, his statements have been universally confirmed. Among the diseases in which this agonal rise occurs, some are characterised by convulsions, like tetanus and epilepsy; in others convulsions and muscular twitchings may be completely absent, as in hysterical paraplegia and tubercular meningitis; in many instances it is in pyrexial affections that these excessive values are reached, either through a slow or rapid rise of the previously moderate febrile temperature, as *e. g.* in cerebro-spinal meningitis or in typhoid with severe cerebral symptoms; in other cases, on the contrary, the bodily heat continues absolutely normal up to the agonal elevation, as in sclerosis of the brain, cerebral hæmorrhage, &c. Since we have here always to deal with diseases which are situated in the central nervous system or involve it during their course, it is certainly not unnatural to place these experiences at the sick bed side by side with the experiments just discussed, a still more marked similarity to which is presented by the surgical illustrations referred to. Wunderlich himself and many later writers attach great importance to the *agonal* appearance of these remarkable elevations of temperature; they believe them to depend on the agony, *i. e.* on the commencing dissolution and the extinction of the brain functions, and thus adopt a standpoint analogous to that of Naunyn and Quincke. Nevertheless, there is no necessity, in my opinion, for such an assumption; on the contrary, we may explain the connection as Senator* has done, and say that the individual dies when and because his bodily heat has risen to such a height that life is no longer compatible therewith. True, this does not relieve us from the task of explaining these unusual elevations of the temperature of the body, a task the solution of which we must postpone till we are furnished with reliable data as to the amount of the metabolism and of the loss of heat during the agonal rise of temperature.

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* Wunderlich, 'A. d. Heilk.,' ii, p. 547; iii, p. 175; v, p. 204.

While we could not previously do more than point out the *possibility* that the increase of temperature after laceration of the cervical cord may at any rate partly depend on the severe disturbance of the circulation through the cutaneous vessels, or on the resulting decrease in the loss of heat, pathology affords us additional opportunities of observing this connection in a clear and incontrovertible manner. I refer chiefly to *cholera*. In this disease the fall in the temperature of the skin, more especially of the extremities, is one of the constant and characteristic symptoms when the attack has acquired a certain degree of violence, so much so that this period has received the name of *stadium algidum*. The cause of this cooling, which for the rest appears more considerable to the hand than it is shown to be by the thermometer, is evident without further inquiry; it is the extreme weakening of the circulation which attends the inspissation of the blood, and which naturally is most pronounced in the peripherally situated vascular areas. The skin becomes pale and cold because the cutaneous vessels are supplied with a much less quantity of blood than normal. But the less blood flows through the cutaneous vessels, the slighter, as you know, is the loss of heat to the surrounding medium, so that consequently a marked *retention of heat* must occur during the stadium algidum. In fact, so considerable is the retention of heat in cholera, that despite all the other truly unfavorable conditions as regards heat-production, *the temperature of the internal parts as a rule rises*, and that by two or three degrees; temperatures of 39° and 39·2° or even of 40° have been repeatedly measured in the rectum and vagina during an attack of cholera.

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* Senator, 'Virch. A.,' xlv, p. 411.

Similar experiences are often met with in patients who have become *collapsed* in consequence of sudden weakness of the heart. Extreme anæmia of the surface of the body and marked coldness of the skin will occur here also, not indeed as the result of inspissation of the blood, but owing to direct depression of the energy of the heart. At the same time there may be a rise of temperature of the internal parts as shown by a thermometer in the rectum; this may often be considerable, especially when the collapse has occurred at the height of a pyrexial disease. Probably many of the agonal elevations of temperature are explainable in this way.

Finally, the same principle underlies a phenomenon which does not properly speaking belong to pathology, inasmuch as it makes its appearance after life has departed—I refer to *post-mortem rise of temperature.* In many bodies, cooling does not at once commence after death; there is first a rise of temperature as measured in the rectum. The elevation is not, it is true, considerable; yet it may amount to half a degree or even more, and is usually marked in proportion to the height of the temperature at the moment of death.* The rise usually lasts only a short time, and gives place at latest in the second hour after death to the definite and now continuously increasing cooling. However paradoxical the post-mortem rise of temperature may at first sight appear, its explanation is very simple; it has nothing to do with any kind of moderating or exciting nervous actions, but is solely *the effect of the persistence of heat-producing processes in the body, while the loss of heat is considerably diminished.* For the chemical processes in the interior of the body, on which the production of heat depends, do not, of course, at once cease with the arrest of the heart's contractions; indeed, an additional source of heat may under certain circumstances be present when rigor mortis sets in rapidly. On the other hand, it is obvious that the cessation of the circulation must greatly reduce the loss of heat. Not only is the loss directly outwards essentially diminished, but the maintenance of the internal temperature is favoured by another circumstance, to which attention has been drawn by Heidenhain,* namely, that the blood previously returned from the periphery no longer mingles with the hot blood of the internal parts. In this way may be easily explained all the above-mentioned details of the post-mortem rise of temperature, which forms an almost constant phenomenon in all large animals, whatever the cause of death—a convincing proof of its independence of any kind of pathological factors.

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* Quincke u. Brieger, 'Deutsch. A. f. klin. Med.,' p. 282.

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* Heidenhain, 'Pflüg. A.,' iii, p. 525.

CHAPTER II.

FEVER.

The essential factor in fever is the rise of bodily temperature.—Classification of fever-temperatures.—Course of a fever.—Pyrogenetic stage.—Rigors.—Fastigium.—The period of defervescence.—Crisis and lysis.—Stage of convalescence.—Daily fluctuations.—Types of fever.—Fever-curves in various acute and chronic diseases.

Causes of fever.—Symptomatic and essential fever.—Experimental fever.—Pyrogenic substances.

Metabolism in fever.—Increased excretion of urea.—Its significance.—Augmented elimination of carbonic acid.—Its significance.—Increased loss of heat in fever.—Inferences as regards heat-production.—Regulation of temperature in fever.—Theories of Liebermeister and Murri.—Perspiration and secretion of sweat.—Cutaneous circulation in fever.—Instability of the bodily temperature.—Behaviour of the nerves of the cutaneous vessels.—The temperature of the skin in fever.—Mutual relations of production and loss of heat in fever.

The individual stages of fever.—Sensation of cold and heat.—Explanation of daily variations and of intermittency.

Other symptoms in fever.—Circulatory apparatus.—Frequency of pulse.—Blood-pressure.—Sthenic and asthenic fever.—Nervous disturbances.—Septic and aseptic fever.—Muscles.—Digestion.—Respiration.—Urinary secretion.—Pathologico-anatomical changes.—Febrile consumption.

Significance of fever for the entire organism.—Possible advantages.—The dangers of consumption, of excessive rise of temperature and of the action of fever upon the heart.—Collapse.

However great the interest and importance of the facts hitherto discussed, it is not to those morbid disturbances of the economy of heat that the prominent *rôle* played by this section in pathology is due. The pathologist, when speaking of disturbances of bodily temperature, has chiefly in mind another process, which formed the subject of careful observation in the earliest ages of medicine, and still continues to make demands on the thought both of practical men and theorists: I refer to *fever*. Both classes have ample grounds for devoting the closest attention to fever. For fever exerts a marked influence on the course and significance of diseases, so much so that its presence or absence in a particular patient becomes a question of cardinal importance at the bedside, and certainly there is no process which so frequently or so essentially determines the physician's treatment. But the more profound the practical importance of fever, the more incumbent is it on theoretical science to elucidate as far as possible the intimate conditions of the process in every direction. Now fever as observed at the bedside presents, it is true, a varying and in many respects complicated picture; and more or less serious functional disturbance of almost all the organs may be present. Nevertheless we are quite justified in treating of fever in this place under the head of the pathology of animal heat; for not only its most constant, but its determining and most essential feature is *the elevation of bodily temperature;* this it is that gives the fever its character. In dealing with the disturbances of the constancy of temperature hitherto discussed, the conditions on which this constancy depends were taken as our starting-point, and though we found that many details were wanting to complete the causal connection, we had in general no difficulty in directly deducing the deviations in the balance of heat from the alterations of the conditions. In studying fever we are still far removed from the attainment of this goal. We shall not, of course, allow any consideration to shake our conviction that the pyrexial increase of bodily heat—in which the influence of a warm external medium is, naturally, out of the question—must depend either on a production of heat so great as to exceed the capacity of the regulative mechanisms of the organism, or on derangement of these mechanisms. But this general conviction is very remote from the accurate knowledge of all the events occurring in the seats of production and loss of heat during fever; yet not till we know these shall we be in a position to really explain the pyrexial rise of temperature. In the present state of our knowledge we are compelled, as in so many other parts of pathology, to adopt an opposite course: we shall for the present abstain from the attempt to deduce the pathological process from the disordered conditions, and shall seek to obtain an insight into its possible or probable conditions by considering the process in all its aspects. We shall, accordingly, commence with an exposition of the state of the temperature in fever, dealing with it only in so far, of course, as it bears on the general doctrine of fever, and omitting more especially all those details which properly belong to special pathology.

In febrile diseases, every degree of rise of temperature is observed, from the lowest, which barely exceeds the normal, to the highest, by which life is directly threatened. The amount of elevation is essentially determined by the intensity of the agent exciting the fever, although individual circumstances must be taken into account. For all persons do not react equally to the same cause, the temperature of one rising more rapidly and to a higher elevation than that of another. Thus we find by experience that the bodily heat of children is very easily increased to a very considerable extent, while that of an aged person will, in the same kind of febrile affection, usually fall short of the temperature found in early life by from half to a whole degree. Notwithstanding this reservation, it has been found desirable, for obvious practical reasons, to arrange the various elevations of temperature occurring in febrile diseases in classes, though the number and gradations of the latter are to some extent arbitrary. Here in Leipzig the classification of Wunderlich is usually followed; according to it, temperatures up to 38° are regarded as *high normal* or *subfebrile;* from 38° to 38·5°, as *low febrile;* from 38·5° to 39·5°, as *moderate febrile;* up to 40·5°, as *pronounced febrile;* above 39·5° in the morning and 40·5° in the evening as *high febrile;* while temperatures exceeding 41° or even 42° are known as *hyperpyrexial.*

Now, as to the course of a febrile disease, it may, according to the nature of the particular affection, present the greatest differences; yet with respect to our present point, namely, the temperature of the body, it is possible, in the acute diseases at least, to distinguish several periods, which recur with more or less sharpness in all of them. The first of these, the period during which the fever is developing, the *pyrogenetic* or *initial stage*, extends from the beginning of the illness to the time of attaining the lowest average temperature characteristic of the particular disease at its acme. Its duration may differ extremely; in particular there are diseases with a very *short* and others with a *prolonged* initial stage. In the former case the bodily heat is rapidly and continuously augmented, and reaches in a few hours or at most within a day the elevation characteristic of the second stage. The shorter this initial period and the greater the increase of temperature during it, the more certainly does the group of symptoms make its appearance, with which you are familiar under the name of "*fever-chill.*" During this, the patients experience a marked sensation of extreme cold; the skin of the face and extremities, especially its peripheral parts, displays a cyanotic pallor, while its temperature is abnormally low, so that it feels cold to the finger; this is less conspicuous on the trunk, which may even be abnormally warm. As so frequently happens, involuntary movements are here associated with the sensation of extreme cold, and may be merely a slight trembling and chattering of the teeth or a violent rigor. The duration of such a painful rigor is fortunately short, and lasts half an hour or at most two hours, very rarely longer,—a period which has nevertheless sufficed to cause a considerable rise of temperature, sometimes amounting to 2, 3, or even more degrees: the chill now gradually disappears, and is immediately followed by the next stage. The greater the number of hours elapsing before this last point is reached, the more moderate will be the manifestations of the chill, even when the initial stage is short, and they are usually altogether absent when the pyrogenetic period embraces several days. In cases of the latter kind the temperature rises *gradually*, and as a rule with slight diurnal fluctuations; there is a slight fall during the early hours of the day, followed by a rise the same evening, and that to a greater elevation than on the previous day. So it goes on till the fourth or fifth day, or longer, till the initial period passes insensibly into the following stage.

In this second stage, the so-called *fastigium*, the fever is at its height. Not that the temperature cannot exceed the elevation present at the end of the pyrogenetic period, or is constantly maintained at that elevation during the fastigium. On the contrary, it is even the rule for the bodily heat to go on increasing during the second stage, and to attain one or even more *acme-like* elevations, after and between which a more or less considerable fall takes place. Even if during this period the temperature is maintained for a short time at a certain uniform height, variations will even then occur, and though sometimes slight, are at other times really considerable. Still it seems justifiable to speak of a high stage of fever while the temperature continues above the limit which marked the termination of the initial period. The fastigium is the period during which the patients themselves have a subjective sensation of abnormal heat; during it no part of the skin feels cool to the touch, and is on the average everywhere warm. As regards duration, the fastigium presents still greater differences than the pyrogenetic stage in the various diseases; in intermittent and in ephemeral simple fever the high stage is over in a few hours, while in enteric fever or in acute articular rheumatism it may occupy an equal number of weeks. That it is the fastigium which is of chief importance as regards the entire course of a febrile disease, need not be shown more minutely. If during this stage the bodily heat does not exceed 39°, the fever will be distinguished as low or moderate; and, on the other hand, it is precisely during the fastigium that the high febrile and hyper-pyrexial temperatures occur, which so often precede the fatal termination.

If the course of the disease be favorable, the fastigium is followed by the third period, the stage of *defervescence*, during which the bodily heat returns to the normal. Like the preceding, the course and duration of this stage present the greatest possible differences. It is most sharply defined when the fastigium with its high temperatures is at once followed by the fall, which may be rapid (*crisis*) or protracted (*sis*). Where defervescence takes place by crisis [illegible] perature declines within some hours—certainly in twenty-four or thirty-six—in a more or less continuous line, by 2°—3°, and in certain circumstances by 5° or even 6°, while *a profuse secretion of sweat* as a rule breaks out simultaneously. It not uncommonly happens that a rapid fall of this kind overshoots the mark, ending in a subnormal temperature, and it may be found that a patient who was yesterday left with a high fever of perhaps 41°, and in a most uneasy state, is today free from all his troubles and with a temperature of almost 36°. On the other hand, defervescence by lysis is much slower and more gradual, occupying three, four, or more days; and here we find a similar state of things to that observed in the pyrogenic stage, namely, that the fall follows either a perfectly continuous or an evidently remittent type; in the latter case there is every evening a rise, which is each day slighter, and every morning a daily increasing fall. But the limit between fastigium and defervescence is not always so sharp; all sorts of irregularities are occasionally observable. Between them there is sometimes interposed a short but not inconsiderable elevation of temperature, the much-discussed so-called *perturbatio critica*; at other times there is a period of indecision lasting some days, a so-called *amphibolic* stage, during which the heat of the body undergoes conspicuous up-and-down oscillations; and in other cases, again, the definitive defervescence is preceded by a brief interval during which the temperature, though already reduced, is still considerably above normal: this is a step preparatory to the decline, which does not itself come off for a couple of days, when it unmistakably sets in either by crisis or lysis.

During the *period of convalescence*, which succeeds the defervescence, the bodily temperature gradually accommodates itself to the normal conditions, provided no special factors conditioned by the disease intervene to hinder it. If it was subnormal at the end of the crisis, the low values are probably maintained for a few days, when the normal temperature with its diurnal variations is permanently re-established; yet in this earliest period a low febrile temperature may appear towards evening. It would seem that the factors on which the constancy of the bodily temperature depends do not, after a severe febrile disturbance, at once discharge their task with their previous promptness and certainty; and in fact the most remarkable peculiarity of the stage of convalescence is that the bodily heat is more *mobile,* unstable, than in health, showing greater daily variations, and undergoing a really considerable rise on slight provocation, such as trifling muscular movements or the first meal of solid food, and the like.

Only too often, however, febrile diseases *terminate fatally,* not uncommonly, as you will soon hear, owing to the febrile rise of temperature; in the great majority of cases death takes place during the fastigium. It is not absolutely necessary that the course of the temperature should be altered when the disease ends unfavorably; there may be nothing in the temperature curve to point to the approaching catastrophe. Much more frequently, however, it changes its character when the fatal turn takes place, though not always in the same way. In very many cases the agony is introduced by a marked and occasionally very considerable fall of temperature; in many others, most remarkable fluctuations are met with, while the approach of death is heralded by a most irregular alternation of the extremest degrees of fever with the lowest subnormal temperatures; and a third modification consists in a continuous increase of bodily heat previous to the end. Some cases of this last category have a special interest, inasmuch as the temperature during the agony finally attains those excessive values which are still fresh in your recollection from our recent discussion.

These are the main features of the alterations of temperature as they occur in acute febrile diseases; but only the main features. Even if we neglect quantitative differences, there are so many peculiarities of detail that the course of the fever may be very dissimilar in the different diseases, and in the different periods of a disease of some duration. In this respect special importance attaches to a point, to which I have more than once alluded, namely the extent of the *diurnal fluctuations.* That in healthy individuals also the heat of the body varies, though only slightly, during the different periods of the day, you are already aware; in adults the daily minimum is reached in the early morning hours and the daily maximum in the late afternoon.* Similar diurnal fluctuations also occur in fever, yet the difference between maximum and minimum is far from being so approximately constant as in health, and varies extremely from insignificant to really considerable amounts. It usually happens, too, especially in severe pyrexia, that the part of the day occupied by the *period of exacerbation* is prolonged at the expense of the *remission*. For the rest, the diurnal fluctuations in fever are generally analogous in point of time to those occurring in health, *i. e.* the acme of the exacerbation or maximum takes place towards evening, while the low point of the remission or minimum occurs in the early morning hours. Yet various deviations from this regular course are met with, such as a change in the respective periods amounting it may be to their complete reversal, *i. e.* morning exacerbations and evening remissions; and the appearance of one or even two secondary exacerbations or remissions is still more frequently observed. I have already referred to the manner in which the daily fluctuations may sometimes influence the pyrogenetic stage as well as the defervescence, when this takes place slowly; their influence is still more strikingly apparent during the fastigium. According as the daily excursions during this period are great or little, it is usual to speak of different *types of fever*. The type is *continued* when the difference between maximum and minimum is very slight, amounting at most to a few tenths of a degree; where the difference is somewhat greater we may speak of *febris subcontinua*; and if, as is by far the most common occurrence, especially in diseases running a long course, the acme of the exacerbations exceeds the low point of the remissions by one or more degrees, the type of fever is termed *remittent*. Contrasting with these we have the intermittent type, which is characterised by *the alternation of periods of high, with intervals of normal or even subnormal, temperature*. In this type each febrile period, or, as it is usually called, each *attack* or *paroxysm of fever* reproduces more or less closely the entire course of a febrile alteration of temperature, having an initial period, a fastigium, and a period of defervescence, while during the apyrexial intervals none of the symptoms peculiar to fever are manifested, so far at least as the temperature of the body is concerned. If, nevertheless, we do not speak in these cases of a number of successive febrile diseases, but of a fever of the intermittent type, this mode of expression is justified by the fact that the successive attacks of fever always depend on a single disease; it is a single, and not repeated infection by the virus of ague or relapsing fever, that is the cause of the entire series of paroxysms.

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* Cf. the numerous measurements of Jürgensen, 'D. Körperwärme des gesunden Menschen,' Leipsig, 1873; Jaeger, 'D. A. f. klin. Med.,' xxix, p. 516.

Nothing, you perceive, could be more erroneous than to assume that the state of the temperature in febrile diseases presents no other differences than are involved perhaps in the intensity and duration of the process. So numerous are the variations that it is quite impossible to give a general description of them. It is, however, enough in my opinion, when studying the pathology of the febrile process, to be aware that such differences in the course, and variations in the type, of fever occur, while a perfect knowledge of all the details is superfluous. He who is face to face with some particular febrile disease, and desires to understand and treat it, must not only know whether fever and what degree of it is present, but will find an accurate knowledge of the course and type of the fever of very special value. In the three decades which have barely elapsed since Traube and Baerensprung first placed the thermometer in the axilla of a patient, there has been accumulated—thanks chiefly to the unceasing labours of Wunderlich—such an endless number of observations on the state of the temperature in the various diseases, that to-day there is perhaps no character or function with the behaviour of which in disease we are so accurately acquainted as the bodily heat. Efforts have been made on every hand to determine whether in a particular febrile disease the initial stage is long or short, whether the type of fever is continued, remittent, or intermittent, whether during the course of a disease one type succeeds another, and whether the defervescence occurs by crisis or by lysis; further, to ascertain how high the temperature rises and how great are its variations in a particular disease or in certain periods of it, how long the fastigium lasts, and on what day from the commencement of the disease defervescence usually begins, &c. In fact, a knowledge speedily began to be acquired that a great number of diseases, especially those which as regards their other symptoms also pass through a more or less regular cycle and then terminate, are characterised by a definite behaviour of the temperature curve which is repeated in all essential particulars in the individual cases. In these diseases, among which I shall only mention typhoid, pneumonia, measles, relapsing fever, this knowledge has grown to be one of the most valuable and reliable aids to diagnosis; yet even as regards maladies, the temperature curve of which does not appear to possess a definite and constantly repeated regularity, an accurate knowledge of the temperature is of indispensable service in properly estimating their course. There is no lack of such affections. Just as in pleuritis, rheumatic endocarditis, and even in diphtheria of the fauces, there is not even an approximate agreement between all the individual cases as regards the course of the symptoms generally and in particular the anatomical changes, so it is also with the pyrexia in these diseases; the anatomical process may stop at any imaginable stage of its development without passing through a prescribed series of alterations, none of which would be absent in typhoid or pneumonia, and similarly there could be nothing more inconstant than the course of the fever, whether in respect of absolute height, type, or duration, &c. And these, remember, are acute diseases. In *chronic* affections any approach to constancy of the temperature curve is quite out of the question. Here it is often impossible to define even the ordinary stages of fever. For since the chronic diseases, unless originating in an acute affection, are wont to develop insidiously and gradually, it is generally impossible to fix on an actual initial period. But it would be no less arbitrary to regard a period of several months, during which the disease continues, as a long fastigium, although the most conspicuous variations of temperature, the alternation of paroxysms of fever with apyrexia, a type at one time continued at another discontinued, point unmistakably to the fact that very different causes may call forth the single febrile paroxysms in the course of the long disease. Finally, should recovery take place, the commencement of defervescence cannot as a rule be distinguished, and it is nothing unusual for several elevations to occur before the definitive decline sets in, which even then takes place very gradually and only by very pronounced lysis.

Now, however thoroughly we may be acquainted with the course of the temperature in febrile diseases, and however certain it is that the heat of the body is increased, this fact alone is quite insufficient to adequately characterise fever. For, as you are aware, the bodily temperature can be raised above normal by a variety of factors, without its occurring to any one to call every such elevation "febrile." We wisely reserve this term for a rise of temperature taking place *under certain circumstances;* we connect with it the *idea of ætiology,* which many may not be conscious of, and which, while it cannot yet be accurately characterised, certainly signifies something more than the mere expression "from internal causes." Accordingly, if we desire to obtain an insight into the conditions of the febrile process, we must first acquaint ourselves with the *causes* of fever, and the circumstances under which it is observed.

In a great number of cases the fever is an associated symptom and supervenes upon some local affection of an inflammatory kind; it is secondary, or, as it is termed technically, *symptomatic.* Should a person from any cause acquire a fibrinous or fibrino-purulent pleuritis, or a pericarditis as the result say of the rupture into the pericardium of a cancer of the œsophagus, or a meningitis in consequence of the perforation of a carious focus of the petrous portion of the temporal, he is certainly at once attacked by fever; fever also sets in when a phlegmonous inflammation or a suppurative arthritis becomes established anywhere; the classical example, however, of such symptomatic fever is that which occurs after severe injuries—so-called *wound-fever.* Inasmuch as in cases of this kind, the cause of the fever is apparently so obvious, there was a time when, influenced more especially by the recently acquired pathologico-anatomical facts, a number of writers were unwilling to recognise any other fever except this symptomatic one. Instead of resorting to unbiassed observation, they did not hesitate to delude themselves by such statements as "fever is inflammation become general" into an appearance of understanding; while others, better trained in scientific methods, believed, like Zimmermann,* that the increased heat of the body might be referred solely to the excessive heat-production at the seat of the inflammation. To-day, now that we know that an abnormally great amount of heat is not produced in the inflammatory focus (cf. vol. i, p. 277), we can afford to pass over the theoretical reasons which are opposed to such a view. Yet the connection between inflammation and fever proves, on more close examination, to be even less intimate than might perhaps appear from the foregoing remarks. Not only can true and indubitable, and moreover really severe, acute inflammations, such as nephritis, occur unaccompanied by fever, but there may be no increase of bodily heat in exquisitely purulent acute inflammation. A person on whom amputation has been performed and the stump treated without antiseptics may have profuse suppuration, but has usually no fever; and similarly the making of an ample incision into a part undergoing phlegmonous suppuration is, as a rule, followed by a complete fall of temperature, although the suppuration goes on actively enough.

While it is accordingly evident that fever cannot be regarded as simply a function of inflammation or suppuration, we find additional proof of this in the extensive group of fevers which run their course in the absence of any concurrent inflammatory affection, or if such be present, without any dependence upon it, and to which therefore the old expression "*essential*" might be applied. I refer, I need hardly say, to the *febrile infective diseases*. For in a number of them, *e.g.* typhus, relapsing fever, and the malarial affections, inflammatory processes are completely absent when the disease is uncomplicated; in a number of others, such as enteric fever and smallpox, though necrotic and purulent foci make their appearance during the course of the disease, they are not related to the fever and develop only after this has reached its acme; and if in scarlet fever and measles a widespread but not *per se* severe inflammation of the skin is established, so little is this the cause of the high fever, that it does not precede but invariably follows the rise of temperature. Moreover, in genuine pleuro-pneumonia, no demonstrable relationship of dependence subsists between the inflammatory infiltration and the fever; as a rule the rigors introduce the disease in its entirety, while, on the other hand, the inflammation often continues, and may even progress, after the crisis is passed. Finally, it is doubtful even whether the fever of cerebro-spinal meningitis or of acute rheumatism is really secondary and dependent on the local inflammatory affection, and not rather equivalent to the fever of enteric and of the acute exanthemata.

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* Zimmermann, 'Deutsch. Klinik,' 1862, Nos. 1, 41, 44, 1863; Nos. 43—49.

On now inquiring by what means all these infective diseases and so many local inflammations give rise to a febrile elevation of bodily heat, we again find that experiment has prepared the way for a discussion fruitful of results. Billroth* and C. O. Weber,† with whose names is associated this advance, so extremely important for the whole doctrine of fever, found, contemporaneously and independently, that *animals are attacked by fever when a decomposing animal or vegetable substance is introduced into the subcutaneous cellular tissue or directly into the blood.* Such an experiment, which is best carried out on large dogs or other large animals, runs somewhat the following course. Soon after the injection the dogs grow uneasy, and either lie cowering or are very restless; many become cold and tremble; after an hour or two, and rarely later, the rectal temperature begins to rise, and reaches its acme in four or five hours. At the elevation then attained—1, 1·5°, or 2° and even more above normal—the bodily heat is maintained for some time,—in the worst cases till the approach of death, which takes place three or four days after the injection; in more favorable cases, for eight to ten, or twenty-four to thirty-six hours, whereupon the temperature gradually declines till the normal values are re-established. Whether the course is favorable or not depends for one thing on the quantity of material injected, but still more on its composition: the more putrid it is, the greater will be the danger to life, while we may count with some degree of certainty, on the other hand, on producing a more or less violent fever indeed, yet no threatening putrid intoxication, if we employ fresh good pus, the so-called *pus bonum et laudabile*, purulent sputum, the juice expressed from an inflamed organ, or blood obtained from a fever patient. For the rest, the serum alone of pus suffices to excite fever, nor does the pus lose its *pyrogenic* capacity on being dried at a gentle heat and then diffused in water; it causes no elevation of temperature, however, when it has long remained stagnant in the body, when it has undergone fatty degeneration, become inspissated, or acquired the characters of the contents of so-called cold abscesses. From these facts it may logically be inferred, I think, that the products of acute inflammation, more especially when purulent, contain at a certain period one or more substances, which, *on entering the circulation*, give rise to a febrile elevation of temperature. In this way the secondary or symptomatic fever is ætiologically explained, while its occasional absence under apparently identical conditions is also rendered intelligible. For to produce fever, *the pyrogenic substances* must not only be present, but *must be absorbed into the juices of the body*. Absorption follows most certainly when the products of inflammation are contained in the close meshes of a little distensible tissue and are consequently under considerable tension; it usually completely fails to take place when the inflammatory products are free to escape, as in nephritis or an amputation stump treated without dressings; and since an incision into a suppurating part allows the free passage of the pus from its place of production outwards, further absorption and consequently the fever are terminated by it.

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* Billroth, 'Langenbeck's A.,' ii, p. 325; vi, p. 372; xiii, p. 579.

† C. O. Weber, 'Berl. klin. Wochenschr.,' 1864, No. 39; 'Deutsch. Klinik,' 1864, Nos. 48—51; 1865, Nos. 2—8.

There has been no want of investigations* into the nature of the pyrogenic substances since the early experiments of Billroth and Weber. The first question—whether the effect is produced by cells contained in the exudation—was indeed soon settled, by the fact already mentioned, that the serum of pus is active, and no less by the pyrogenic properties of animal and vegetable putrid fluids. But when we at present contrast a dissolved with a corpuscular agent in the inflammatory products, it is not with reference to the cellular elements of our bodies, but to *lowly organisms;* and their possible participation is the more deserving of consideration, as it is pre-eminently the inflammations with purulent exudation that are distinguished by an energetic pyrogenic capacity. So soon as we adopt the notion of throwing the responsibility of the fever on the exciters of inflammation contained in the inflammatory products, we at one stroke open the path to the febrile infective diseases, which, you know, owe their origin solely to the invasion by schizomycetes. And is there not, in truth, something very seductive about this view, when one observes the rise of temperature in the paroxysm of relapsing fever to follow immediately the appearance of spirilla in the blood, and the disappearance of the latter to directly precede the decline of temperature? But even so, it would still have to be decided whether it is the schizomycetes themselves or certain chemical substances produced in and by their metabolism that give rise to the fever. Senator[*] is disposed to adopt the latter alternative, because he succeeded in obtaining a strong pyrogenic extract from sputum by means of glycerine; and Klebs and Tiegel[†] also are supporters of the same hypothesis, since they were able to set up violent fever in a rabbit by injecting an infusion prepared from a pneumonic lung, from which they believe they had excluded all bacteria by filtration through earthenware cylinders. Still it is greatly to be wished that we could support this view by unexceptionable evidence, and in particular by the isolation of the active principle itself. For the moment we may indeed neglect this secondary question, all the more so as true fever may undoubtedly originate *without the co-operation of schizomycetes.*

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* Cf. more especially Bergmann, 'Petersb. med. Zeitschr.,' xv, 7 and 8, 1867; Frese, 'Experiment. Beiträge zur Aetiologie d. Fiebers,' Inaug.-Dissert., Dorpat, 1866; Klebs, 'Correspondenzbl. f. schweiz. Aerzte, 1871, No. 9.; Tiegel, 'Ueber d. fiebererregenden Eigenschaften d. Mikrospor. Sept.,' Inaug.-Dissert., Bern, 1871; in Klebs' 'Arbeiten aus d. berner patholog. Inst.,' 1873, p. 130; Senator, 'Med. Centralbl., 1873, p. 84; Kehrer, 'A. f. experim. Patholog.,' ii, p. 33.

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[*] Senator, Med. Centralb.,' 1873, p. 84.

[†] Tiegel, 'Ueber d. fiebererregenden Eigenschaften d. Mikrospor. Sept.,' Inaug.-Dissert., Bern, 1871; in Kleb's 'Arbeiten aus d. berner patholog. Inst.,' 1873, p. 130.

After an injection of lamb's blood, the unfortunate patient is always attacked by a more or less violent paroxysm of fever, and the same thing may be observed in a dog into which you have introduced a fairly large quantity of ox's or cat's blood, although by direct conduction from the carotid into the femoral vein you have excluded all contamination by schizomycetes. Unmistakable fever is also occasionally observed after the injection of large quantities of distilled water and of solutions of certain poisons, *e. g.* ammonium sulphide. But why seek for such unusual and some of them singular examples, when wound fever daily affords a most convincing demonstration that fever may arise without the co-operation of bacteria? It is indeed true that those severe septic fevers which were at one time the dread of the wounded and of the physician have now practically disappeared from the list of our diseases, thanks to the abounding benefits of Lister's discovery. But Volkmann* has with good reason recently drawn attention to the fact that healing may be antiseptic and yet wound fever occur. Despite the most perfect antiseptic treatment and the most regular and rapid healing of the wound, it is anything but rare for the bodily temperature to attain an elevation of 40° or more; and should it be objected to this that the settlement of bacteria in a wound is not absolutely excluded by Lister's treatment, all doubt on this ground is dispelled by *subcutaneous* injuries, *e. g.* by simple fractures of bone and contusions of joints. If in Volkmann's clinic, of fourteen ordinary fractures of the femur, no less than eleven were accompanied by more or less violent and persistent fever, which in five patients amounted for several days to between 39° and 40°, and in four lasted more than ten days, any discussion as to whether fever is always an effect of lowly organisms is quite indefensible.

Yet one cannot fail to perceive that in these cases also a condition has been established in which foreign, unrelated, and moreover readily decomposable substances may enter the juices of the physiological organism. For every severe trauma must necessarily be attended by a destruction of some kind of tissue-elements, sometimes to a ve and whether we have in these cases to deal chiefly with blood-clots, lacerated medulla of bone, ruptured muscles, or necrotic adipose tissue, all the broken-down and mortified masses disappear by means of absorption, wholly during the healing of subcutaneous wounds, and in great part at least where the skin has been broken through. The transfusion of blood from a different species is, you are aware, equally attended by a rapid destruction of numberless blood-corpuscles, and the poisons giving rise to fever also probably exert without exception a deleterious action, whether on the elements of the blood or on the tissues of the body with which they come into contact. Under these circumstances, we shall not be likely to err if we attribute the fever in these cases to the entrance into the juices of the body of the *products of an acute disintegration of the tissues*, in large quantities. Among the products there may be a number of very different substances according to the structure and composition of the dead tissues. You no doubt remember, from our former discussions on the coagulation of the blood as well as on coagulation-necrosis (vol. ii, p. 563), the facts which render it highly probable that, during the destruction and disintegration of protoplasmic cells, foreign substances are as a rule set free, which in their behaviour and properties either completely agree with or are closely related to Alex. Schmidt's *fibrin-ferment* of the blood. To this ferment the attention of the Dorpat school, to which our chief knowledge of it is owing, has been directed as bearing on the ætiology of fever, its possible relations to elevation of the bodily temperature having been submitted to the test of experiment. Experimental investigation showed, in fact, that *the injection of pure solutions of fibrin-ferment*, which were not so concentrated as to cause immediate extensive coagulation in the vascular system (cf. vol. i, p. 239), gave rise in the animals experimented on to a number of severe symptoms recalling putrid intoxication, with *a rapid and very considerable elevation of temperature*. That Edelberg,* the originator of these interesting experiments, should feel himself justified in asking on the strength of them, whether pathological fever is not always connected with the presence of large amounts of fibrin-ferment in the blood is intelligible enough. Yet much evidence must be accumulated before we can answer this question in the affirmative. At present it will be judicious to admit unreservedly that we are not in most cases exactly acquainted with the actual cause of the fever; while at the same time the analysis of the categories of fever occurring pathologically shows that their onset is always preceded by the entrance into the lymph- and blood-circulations of what we may call in general terms, *a noxious agent*, and that the fever may to some extent be regarded as the reaction of the organism to the noxa which has entered it. Yet this agent we are unable to characterise, however unscientific this may sound, except by its capacity of exciting fever; at most we may add that it is *organic* in nature. What we in some measure know are the general conditions in which the agent originates; for we are aware, in the first place, that it is formed under the influence of many infective schizomycetes, either as the product of their own metabolism or in consequence of their action on the animal organism; and, in the second place, that it makes its appearance without the intervention of bacteria, when tissue-elements of our organism are rapidly destroyed in large quantities—as *fibrin-ferment*—hence frequently in non-infective inflammations. But supposing that we were much more accurately and completely acquainted with the nature and properties of the pyrogenic agent than is at present the case, we should still require to explain the febrile rise of temperature. For any idea that the elevation of temperature is perhaps the consequence of the oxidation of the pyrogenic substance itself is—to say nothing of other objections—at once excluded by the fact that minute quantities, a few cubic centimetres, of pus or sputum, suffice to produce severe fever in a fairly large dog. If the introduction into the body of such quantities as this may cause a rise of temperature of several degrees, it can only be by the action of the agent on the factors which control the heat-equilibrium of the organism. We must examine how these factors react to the agent exciting the fever, if we desire to obtain an insight into the origin of the febrile temperature; in other words, the task of investigating the *state*

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* Genzmer und Volkmann, 'Volkmann's
also Edelberg, 'D. A. f. Chir.,' xiii, p. 62.

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* Edelberg, 'A. f. exper. Patholog.,' xii, p. 283.

of the production and loss of heat during fever must be undertaken.

To determine the amount of heat produced during fever, the methods employed to this end in healthy men and animals are available. We can either measure the amount of heat given off during a certain period calorimetrically, and, taking into account any alterations of bodily heat occurring during the same time, we may calculate the heat-production, or we may determine the amount of heat produced in a measure indirectly by examining the oxidative processes taking place in the body during the given interval, these processes being the only sources of heat in the febrile organism also. Both these methods have been followed for several decades by a number of writers, and though still remote from our goal, we are in possession of some valuable facts in this domain. As regards the *metabolism*, in the first place, there was till lately a complete dearth of systematic experiments on the oxygen-consumption in cases of fever, and it is only a very short time since we were supplied with some results bearing on this highly important point. On the other hand, a proportionately large number of writers have undertaken the task of investigating the final products of the metabolism in fever. As regards the nitrogenous products, the results of all investigators are in most satisfactory agreement.* For in every fever without exception, whether symptomatic or essential, whether its course is typical or atypical, whatever its type, whether in the initial stage, fastigium or period of defervescence, *the excretion of the nitrogenous constituents of the urine is increased*, the increase involving chiefly the *urea*, but also the uric acid and kreatinin. Obviously, this result will not appear in a proper light, except the remaining factors which influence the excretion of nitrogenous matters, and chief among them the consumption of food, be taken into account. Values such as are found in a healthy person who consumes large quantities of meat, are seldom attained by the urea-excretion of a fever-patient; but the latter will be found to be in excess, when compared with the urea excreted by a healthy person *on the same diet*. The absolute amount of this increase of urea is, it is true, irregular. Some have believed themselves justified, on the strength of very numerous and careful estimations, in laying down the rule that *the amount of urea-production in general keeps pace with the elevation of the temperature*. Others, however, have failed to convince themselves of the correctness of this rule, which is chiefly upheld by Huppert; moreover, in fevers of a remittent or intermittent character, the only mode in which urine can be obtained in man does not admit of our forming any certain opinion as to the relations between the bodily heat and the condition of the urine. That considerable deviations from the above rule occur, is confessed by Huppert also. Thus, in very badly nourished individuals, the production of urea may be slight despite the presence of the high fever; and while, on the one hand, the most abundant urea-excretion does not usually occur at the commencement of the fever but during the next few days, even though the temperature has not altered and has certainly not increased, we observe, on the other hand, that in cases of prolonged fever there is a reduction in the production of urea, although no fall of bodily temperature has yet occurred. Lastly, during the stage of defervescence, the urea-excretion not uncommonly increases, and in febrile diseases which terminate by crisis it is almost the rule for an abundant so-called *epicritical* increase of urea to take place during the couple of days following the crisis when the temperature is perfectly normal. This is certainly independent of the consumption of food, and can hardly be attributed to an inundation of the organism with urea during the fever; it tells rather for the belief that the increase of albuminous waste brought about by the exciter of the fever is not completed at the crisis, or at any rate that its final products were not then produced. But the greater the number of factors influencing the amount of the urea-increase in fever, the more intelligible is the irregularity in its absolute value, to which reference was already made. The increase may be only extremely trifling or may amount to *three times the normal value*. It is indeed nothing unusual for a young and vigorous man suffering from an acute disease to evacuate *pro die*, despite the strictest fever-diet and smallest amount of food, as much as 40—45 or 50 grams urea or even more,[*] while a person with normal temperature taking the same diet would at most produce 16—18 grams in the twenty-four hours. To lay down average values where the conditions are so extremely unlike is always a dubious proceeding, yet many writers have attempted, on the basis of a smaller or larger number of observations, to fix the average increase of urea; thus Liebermeister[†] has found an increase of 70 per cent., Unruh[‡] precisely the same, while Senator[§] has observed an average of more than 100 per cent., *i. e.* an increase to at least double the normal.

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* Traube und Jockmann, in Traube's 'Ges. Abhandl.,' ii, p. 286; Huppert, 'A. d. Heilkunde,' 1866, p. 1, contains numerous references to the older literature; Riesenfeld, 'Virch. A.,' xlvii, p. 130; Unruh, ibid., xlviii, p. 227; Naunyn, 'A. f. Anat. und Physiol.,' 1870, p. 159; Senator, 'Untersuchungen,' p. 94, *et seq.*; Schultzen, 'Charité-Annalen,' xv, p. 168.

No doubt can be entertained as to the significance of this increased excretion of urea: it proves that *an increase of the disintegration of albuminous substances* takes place in the organism, and since these substances are not introduced as food, that the disintegrating albumen is that of the body itself. We may assert this with absolute confidence, because it is utterly impossible to explain the augmented excretion on the supposition that the urea previously produced has been stored up in the organism. I will not say that the production and excretion of urea always take place exactly *pari passu*; the amount of water-excretion will more especially exert a certain amount of influence on the excretion of urea. Yet an actual storing up of this easily diffusible substance is quite out of the question, and the entire amount of urea which under the most favorable circumstances can be contained in the tissues would not even suffice to cover the increase of urea-excretion during a febrile period of twenty-four hours' duration, to say nothing of a fever lasting several days or weeks. Gscheidlen,[‖] moreover, has convinced himself by direct estimation that in dogs in which fever is set up by the injection of pus, the urea-contents of the blood and different organs do not, during and subsequently to the fever, show any departure from the normal and are certainly not diminished. Whether all the organs and tissues of the body share in the increase of albuminous waste, and if not, which are chiefly preferred, we are not yet able to say with certainty; I shall shortly make you acquainted with the few indications we possess on this point. A still more interesting question perhaps is the relation between the augmented albuminous waste and the rise of temperature. According to the experiments of Naunyn[*] and Schleich,[†] recently discussed, we cannot at once reject the possibility that the increased production of urea is simply the result of the augmented bodily heat, and from this point of view the parallelism supposed by Huppert to exist between urea-production and height of temperature would have still greater fundamental importance. Yet the fact that in very many cases the curves of urea-production and of bodily heat are very far from running parallel appears to me clearly to tell against the existence of so simple a relationship of dependence. Moreover, this view is directly disproved by the evidence obtained by Naunyn[‡] in the septic fever produced by injecting ichorous fluid into a dog; for he found that *the increase of the urea-production takes place as early as the latent period of the fever*, *i. e.* previously to the marked rise of temperature.

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[*] Senator, loc. cit., p. 97.

[†] Liebermeister, 'Handb.,' p. 315.

[‡] Unruh, loc. cit., p. 268.

[§] Senator, loc. cit., p. 101.

[‖] Gscheidlen, 'Studien über d. Ursprung des Harnstoffs im Thierkörper,' Leipzig, 1871.

To regard the increased urea-production in an opposite light, as a source of the over-production of heat is still more open to objection. For it proves simply that larger quantities of albumen are undergoing disintegration, while affording no information as to the actual heat-forming oxidative processes. Hence for our purpose, that portion of the metabolism whose final products are water and carbonic acid has incomparably greater importance. The *respiratory exchange of gases in fever* has during the last ten years formed the subject of many investigations, both in man,[§] and also in animals.* The former present the great advantage that various febrile diseases can be included in the range of the investigation, but, on the other hand, only rarely afford an opportunity of examining the initial period, and in particular very imperfectly admit of a comparison between the interchange of gases taking place in the same individual during fever and in the absence of pyrexia. In dogs, on the contrary, the last-mentioned drawback does not exist, but to counterbalance this advantage the only fever that we can examine in them is that produced by injections of pus or the like, *i. e.* the *septic.* It is the more matter for congratulation, therefore, that despite these various desiderata, all the investigations—among which these of Leyden are pre-eminently distinguished by the number and length of the experiments, the reliability of the apparatus employed, and the cautious estimation of all the conditions requiring to be considered—lead essentially to the same result, and prove that *the excretion of carbonic acid is increased during fever.* The greatest increase, to two and a half times the normal, was observed by Liebermeister during the fever-chill, which, in view of the strong muscular movements of the rigor, will cause you no surprise. Yet Leyden was able, even when the fever did not begin with a chill, to determine the augmented elimination of carbonic acid during the initial stage, so soon as the bodily heat of the animals was at all notably increased. The increase persists throughout the fastigium, and is the more marked the more the temperature exceeds the normal. In man, Leyden found on the average an increase of CO_2-elimination to about one and a half times the normal; Liebermeister saw, at the acme of the fever, an excess of 19—31 per cent., and, while the temperature was rising, but in the absence of rigors, 30—40 per cent. In the dog, Senator observed on the average an increase of 37 per cent., and never saw more than 57 per cent.; Leyden, on the other hand, in whose animals the fever was greater, found an increase of 70—80 per cent., as compared with the CO_2-elimination of a dog which has fasted for an equally long time with the febrile animal; the same observer found, it is true, only 40—

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[*] Naunyn, 'A. f. Anat. und Physiolog.,' 1870, p. 159.

[†] Schleich, 'A. f. experim. Patholog.,' iv, p. 82.

[‡] Naunyn, loc. cit.

[§] Leyden, 'D. A. f. klin. Med.,' vii, p. 536; Liebermeister, ibid., viii, p. 153; 'Handbuch,' p. 321, *et seq.*; Wertheim, 'Deutsch. A. f. klin. Med.,' xv, p. 173; 'Wiener med. Wochenschr.,' 1876, Nos. 3—7; 1878, Nos. 32—35.

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* Senator, 'A. f. Anat. u. Phys.,' 1872, p. 1: 'Untersuchungen,' Cap. 1; Leyden und Fränkel, 'Virch. A.,' lxxvi, 1

50 per cent. on an increase of bodily heat of about 1.5°, and still less when the fever was slighter. In the stage of defervescence, the excess of carbonic-acid excretion gradually becomes less and less as the temperature falls; there is no fresh epicritic augmentation, such as occurs with the urea.

While one is at first sight inclined to regard this increased elimination of carbonic acid as a certain proof of the augmentation of the oxidative processes during fever, Senator has sought to show that the more abundant carbonic-acid excretion in fever might depend on the yielding up by the organism of a greater portion of its store without any increase of production. There is the more need to consider this possibility here as a number of factors are present in the febrile organism which greatly facilitate the excretion of the carbonic acid contained in the blood. Amongst these he counts the greater difference between the temperature of the body and that of its surroundings, which is known to favour all processes of dissociation; further, the increased frequency of the respirations, and lastly, the probable increase of acid-production in the blood, taking place *pari passu* with the rise of temperature. That these factors are actually present during fever and act in the manner claimed, has been proved by an investigation of Geppert,* who found that in septic fever the carbonic-acid contents of the blood of a dog were abnormally reduced in proportion to the elevation of temperature. Since, however, this decrease never sets in till the fever has lasted some time, and is absent in the earliest period, Leyden and Fränkel have probably hit upon the true view, when they refer only a small fraction of the excessive elimination of carbonic acid during fever to the more favorable conditions of excretion. That any greater importance attaches to this factor is rendered improbable, in the first place, by the duration of the increased carbonic-acid excretion, which is conterminous with the whole course of the febrile disease, and which, in my opinion, only becomes intelligible on the assumption that the production of this gas is increased in an equal degree. Furthermore we are acquainted with no other case where this point has been investigated, in which a *lasting* increase in the elimination of carbonic acid is not at the same time associated with a corresponding increase of oxygen-absorption, and there is therefore from the start no justification for substituting another relationship in fever, so long as direct estimations of the oxygen absorbed do not prove its existence. As already remarked, we were not till recently in possession of systematic estimations of the oxygen-absorption, or rather we were acquainted with only a single observation on this subject, which Colasanti[*] incidentally made—by a very exact method, it is true—on a guinea-pig with fever, during an investigation into the dependence of the amount of the metabolism on the temperature of the surroundings. This one observation, however, gave positive results, inasmuch as with only a moderate degree of fever, an increase of CO_2-elimination by 24 per cent. together with an augmentation of oxygen-absorption of 18 per cent. was determined. This single experiment has since then been supplemented in a very desirable way in two laboratories by the independent researches of Zuntz[†] and D. Finkler,[‡] and though, it is true, we are as yet in possession of only a summary of their results, both researches agree in showing, that *in the septic fever of the rabbit or guinea-pig the absorption of oxygen and excretion of carbonic acid are considerably increased, and almost to an equal extent.* Since, however, a moderately persistent augmentation of oxygen-absorption without an increase of *the oxidative processes* is inconceivable, we are justified in concluding that these processes *are considerably intensified in fever.*

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* Geppert, 'Ztschr. f. klin. Med.,' ii, Hft. 2.

Whether and in what degree the formation of water by the oxidation of hydrogen is increased in the metabolism of fever-patients, on this point we have no information, if for no other reason, because we are unable to distinguish between this water, produced by the organism itself, and that which passes through the body after having been introduced as such from without. The investigations hitherto carried out on the total excretion of water in fever are not free from considerable sources of error; and even had they yielded more trustworthy results than is actually the case, they would not allow of our coming to any absolute conclusion, since we are quite uninformed as to whether the water-contents of the tissues and organs are altered in fever. Meanwhile we may here safely disregard the water, because the increased formation of carbonic acid, proved to occur, is itself sufficient evidence of the *excessive heat-production in fever*. What had been guessed at by the older physicians or inferred for reasons to which we do not now attach any weight, is to-day indubitably established; and we might unhesitatingly affirm the foregoing law on the strength of investigations into the metabolism, even did no calorimetric estimations exist, whose results, as you will soon hear, are in complete conformity to it. But however unquestionable the fact that in fever the heat-production is relatively increased as compared with the non-febrile condition, this alone does not throw much light on the febrile rise of temperature. Taken absolutely, the augmentation of the heat-producing processes is not at all great. For the albuminous waste and hence the excretion of urea of a fever-patient may, it is true, nearly approach that of a healthy person taking a fair or even an abundant supply of food; but, as correctly dwelt on by Senator, the actual oxidative processes in fever are not augmented in the same degree as is the disintegration of albumen, and certainly the greatest observed increase of CO_2-elimination falls much short of that which takes place in a healthy person, who has consumed a large quantity of food, especially if rich in fat, or, still more, who is undergoing forced muscular exertion. But if during such abundant heat-production the temperature of a healthy person remains unchanged, or at most rises a few tenths of a degree, why is not this also the case in fever patients? You know the means whereby the healthy avoid the disturbing effects of increased heat-production; it is by a corresponding augmentation of the loss of heat. To this conclusion we are inevitably compelled. If with the same original temperature and the same production of heat, one individual maintains the bodily heat at its previous elevation, while the other develops three to four degrees of fever, this cannot possibly be due to anything but an inequality in the amount of heat lost. The ways and mechanism by which the loss of heat is effected in health are known to you; let us now see what we know of the amount of loss in fever and of the behaviour of the factors which are concerned in it.

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[*] Colasanti, 'Pflüg. A.,' xiv, p. 125.

[†] Zuntz, 'A. f. Physiolog.,' 1882, p. 115.

[‡] D. Finkler, '[illegible] vii, p. 267.

The question of the *loss of heat in fever* has already a history. The older pathologists had regarded it as self-evident that, corresponding to the greater difference in temperature between a fever patient and his surroundings, more heat is given off by him. Then in the sixth decade of this century, Nasse and Fick pointed out that a diminution of the loss of heat, even in the absence of any increase of heat-production, indeed despite a possible decline of the latter, can raise the temperature of the body. Yet to Traube unquestionably belongs the great merit of having given this factor the place which it deserves precisely in fever. In a carefully matured theory in which no side of the fever process was neglected,* he has attempted to deduce the febrile rise of temperature only and solely from the diminished loss of heat, which itself depends on the vigorous contraction of the small arteries supplying the peripheral parts of the body with blood. When the agent exciting the fever acts with great intensity on the vaso-motor system of nerves, whether owing to the great excitability of the latter or because the agent has entered the blood in large quantities at once, there takes place a rapid increase of bodily heat, while, on account of the rapidly developing difference of temperature between the peripheral and central terminations of the sensory nerves, a *rigor* occurs; if, however, the excitation of the vaso-motor nerves is feebler and only very slowly reaches its acme, the pyrogenetic stage extends over a longer period; similarly, the rapid relaxation of arterial tone corresponds to the rapid decrease or crisis of the fever, the slow relaxation to the lysis. Great was the sensation created by this doctrine; yet from the very first it met with opponents, who, while admitting the ingenuity of the conception and its skilful application to all the details of fever, yet refused their assent to the cardinal point, the asserted diminution of the loss of heat. Traube himself had not proved the occurrence of a diminution by positive observations, but had merely inferred it from certain phenomena, in particular, of the fever-chill. For a number of other writers, the doctrine formed an incentive to an examination by suitable methods of the loss of heat in fever. Liebermeister,[*] Hattwich,[†] and others have carried out such observations by placing fever-patients in baths of water, and have found that more heat is given off by them to a measured quantity of water of accurately known temperature than in health. More importance attaches, however, to the numerous measurements carried out by Leyden[‡] in various febrile diseases, because these take into account not only the loss of heat by conduction, as in the bath-experiments, but the loss by evaporation also. In carrying them out, he employed a suitably constructed calorimeter, into which was introduced not, it is true, the entire body of the patient, but a considerable portion of it, namely *one leg*, and this was allowed to remain in it on each occasion for two hours. He found as the result that *the loss of heat in fever is considerably increased as compared with the normal.* Finally, Senator[§] has calorimetrically determined the loss of heat in dogs rendered febrile by injections of pus, and found that it is increased at the acme of the fever, though less markedly than was the case in Leyden's patients —a difference easily explained by the much slighter elevation of temperature in the dogs.

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* Traube, 'Ges. Abhandl.,' ii, p 637.

While, accordingly, the different authors are perfectly agreed that more heat is lost to the surrounding medium during fever than in health, it is no less certainly established that *the absolute amount of loss is very unequal in the different febrile phases.* Leyden's figures are the most instructive in this respect, though those of other writers do not essentially differ from them. The loss of heat is greatest during the period of defervescence, and here, especially during the critical fall of temperature, it may amount to twice or three times the normal. The least degree of loss occurs during the initial stage; when this stage is short, the loss only slightly exceeds, and may during the chill be less than, the normal. During the fastigium, lastly, the increased loss of heat may in high fever amount, on the average, to from one and a half times to twice the normal. I say on the average; for it is precisely in this stage that the most conspicuous fluctuations are apparent, and that too without any corresponding change in the temperature of the body. It has been repeatedly determined that the loss of heat during moderate and rather high fever temperatures was less than when the temperature was lower; and one may convince one's self of the occurrence of such fluctuations not merely in different persons, but in one and the same patient during the course of a febrile disease.

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[*] Liebermeister, 'Aus d. med. Klinik zu Basel,' Leipzig, 1868, p. 121.

[†] Hattwich, 'Ein Beitrag z. d. Untersuchungen über d. Ursachen d. Temperatursteigerung in fieberhaften Krankheiten,' Inaug.-Dissert., Berlin, 1869.

[‡] Leyden, 'D. A. f. klin. Med.,' v, p. 271.

[§] Senator, 'Untersuchungen,' Cap. 1, and p. 137. Similar results have been obtained by Wood ('Fever,' p. 166, *et seq.*) by experiments on dogs and rabbits.

These fluctuations do not, however, militate against the fact that the loss of heat is increased throughout the fever, and since this increased loss coincides with a rise of bodily temperature, it affords a welcome confirmation of the results arrived at by investigating the metabolism, and proves that there is *an increase of heat-production during fever.* This conclusion is unassailable as regards the fastigium, and no less so for the period of rising temperature, when the loss of heat is augmented during it: on the other hand, with respect to the defervescence, especially if rapid, where the greatly increased loss coincides with the rapid fall of temperature, the assumption of an excessive heat-production does not appear justifiable without further evidence, and may, as a rule, be dispensed with. For the stage of chill, however, a calculation first made by Immermann,* and afterwards more thoroughly carried out by Liebermeister,† has shown that *during this period also the production of heat must of necessity be considerably augmented.* Taking the heat capacity of the body to equal 0·83, they found that a person whose temperature has risen during a short fever-chill by 2° or more has experienced a much greater accession of heat than would under normal circumstances be produced; and that, consequently, even the complete cessation of all and every loss of heat, or the most perfect heat-retention, would not be sufficient to bring about the rise of temperature, to say nothing of its actually doing so where the loss of heat during the fever-chill is only a little less than normal. You perceive then that Traube's theory cannot even be maintained for that stage of fever, on the observation of which it was based, and that in its original unqualified form, in which the increase of heat-production was absolutely denied, it is completely disproved. For it is at present positively established that *in fever*, except perhaps during the stage of defervescence, *both the production and loss of heat are increased above the normal*. But by the recognition of this fact, it is clear that the febrile elevation of temperature is not in any degree elucidated; at first sight, indeed, new difficulties apparently crop up. Since an elevation of bodily temperature can only be due to the preponderance of production over loss of heat, the rise of temperature in fever would be equally intelligible if, as Traube assumed, the loss were considerably reduced while production remained unaltered, or if production alone were increased without a simultaneous augmentation of the loss. But how are we to explain matters, since both are in reality increased in fever? In what consists the difference from a healthy person, who compensates for an increase of production only and solely by a correspondingly increased loss, and in this way maintains his bodily heat at a normal elevation? But however contradictory the known facts may appear, you will not be disposed to sacrifice your well-established physical conceptions, the less so as there is a very simple way out of all these difficulties. The bodily heat remains unaltered when the increase of heat-production is attended *pari passu* by a *correspondingly* increased loss of heat, or in other words, when the latter is augmented to the same extent as the former. Thus it is in health; but is it so in fever? Does the increase of loss correspond *quantitatively* to the increase of production? That is the question, or rather—*it is unquestionable that it does not do so.* The rise of bodily temperature proves in a clear and absolutely irrefutable manner that the increase of loss does not keep pace with the augmented production of heat, and it is our business, not to demonstrate the inadequacy of the loss, but to discover the causes owing to which the loss of heat in fever is insufficient; for there is no doubt that the regulation of the temperature in fever is disturbed; it is the nature of the disturbance that requires to be cleared up.

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* Immermann, 'De morbis febrilibus quæstiones,' Inaug.-Dissert., Berlin, 1860; 'Deutsch. Klinik,' 1865, Nos. 1, 4.

† Liebermeister, 'Handb.,' p. 302, *et seq.*

Liebermeister evades the difficulty in a simple and certainly a peculiar way. After carrying his examination to the point where the increase of production and loss of heat are established, he attempts to get over the real problem by saying* that the essence of fever consists in *the regulation being adjusted at a higher degree of temperature than in health.* Regulation goes on in fever, and though not quite so ample as in healthy persons, takes place in the same direction; while the temperature in health is regulated at 37° approximately, the fever-patient maintains a temperature of perhaps 40°. To this view Senator has raised the objection that in fever we observe anything rather than a persistent preservation of a constant temperature, such as is so characteristic of healthy persons; rather, it has been apparent to every observer, since the bodily heat was first systematically measured, that *the temperature in fever is extremely unstable.* This is perfectly true, but does not directly tell against Liebermeister's theory, since it is admitted by him that the regulative mechanisms act less promptly and amply; on the contrary, Liebermeister might point in his own favour to the fact that the temperature in fever always returns to its high elevation despite such fluctuations. The theory, however, does not appear to me to require serious refutation, since at best it has only the value of a paraphrase of the actual facts. But even with this limitation, which is now admitted by Liebermeister himself, I cannot think his view a happy one; for it does not stimulate to renewed investigations, but rather discourages such; moreover, it undoubtedly savours somewhat of mysticism, since it implies that the nature of man may be altered in a moment, and one of its inborn qualities be suddenly converted into that of a bird.

Murri,† on the other hand, attempts a genuine reply to the question engaging our attention. He disputes the existence of any fundamental difference between the heat regulation of a healthy person and of a fever-patient; and if, nevertheless, the latter is unable to get rid of the entire excess of heat, this depends only and solely on the fact that *in fever the production of heat is continuously augmented without the occurrence of any pauses.* The heat-production of a healthy person, whether through consumption of food or as the result of muscular exertion, invariably lasts for only a limited period, and thus allows the body the necessary interval for getting rid of the excess of heat; did analogous pauses in production occur during fever, it would at least be a question whether the temperature of fever-patients would not also return to the normal. This is in fact a really noteworthy point of view, which is supported by some physiological experiences. For we know that an extreme increase of bodily heat may be produced by repeated tetanisation of numerous voluntary muscles; and although we cannot here exclude direct disturbances of loss of heat (cf. vol. iii, p. 1324), I was able to inform you that forced voluntary muscular exertion causes a measurable rise of bodily temperature, which may persist till the body has during rest yielded up the superfluous heat and thus become cooled. Nevertheless, Murri's view does not, in my opinion, suffice to explain the febrile elevation of temperature. The increase of bodily heat does not, as a rule, amount to more than a fraction of a degree during forced muscular exertion, and an increase of a whole degree has only very exceptionally been recorded; in fever, however, we have to deal, not with a rise of one, but of two or three degrees and more. To make the difference still more conspicuous, the amount of carbonic acid which is produced even in high fever does not remotely compare with that which is eliminated by a person undergoing severe physical exertion. Accordingly, it is absolutely incorrect that a healthy person gets rid of his superfluous heat only in the intervals of rest; rather the loss so preponderates during exertion, *i. e.* simultaneously with the plus heat-production, that however great the latter may be, the body becomes at most one degree warmer, and usually not even so much. However willingly we admit that Murri's explanation is based on a correct idea, it is obviously impossible to avoid concluding that the factors on which the loss of heat depends do not in fever act with physiological promptness and energy, but behave in some way faultily.

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* Hanbd., p. 357, *et seq.*

† Murri, 'Sulla teoria della febbre,' Fermo, 1874.

Such a fault was pointed out by Leyden* in one of his earliest papers on fever, namely, the change in the *evaporation of water*. The rule of the healthy physiological condition is that a rise of superficial temperature is followed by increased evaporation from the skin, but this rule does not hold in fever. During the fastigium the perspiration is in general somewhat augmented as compared with the normal, so that the increased loss of water from the skin and lungs alone explains the diminution in volume of the urine; yet this augmentation of the insensible perspiration does not correspond to the degree of rise of temperature. In the fever-chill, moreover, the perspiration is even reduced below the normal. These relations are still more strikingly apparent as regards the *secretion of sweat;* though this, it is true, is a subject which still needs to be cleared up. In healthy persons who are free from fever, every rise of the temperature of the blood is responded to by a profuse secretion of sweat, but *the great majority of fever-patients do not sweat,* not merely during the chill stage, but during the fastigium at the acme of the fever, the secretion only setting in on the fall of bodily temperature; and this contrast is rendered the more enigmatical as there are a number of febrile diseases, like acute rheumatism, trichinosis, acute miliary tuberculosis, in which a copious secretion of sweat often appears at the height of the fever. As to the cause of the dissimilar behaviour of the secretion, we are so far uninformed; and certainly no pathologist can be satisfied with the suggestion of Luchsinger,† that a defective irritability and depression of the nervous system accompanies those fevers, in which, during the fastigium, no secretion of sweat sets in. We must at present be content with the fact that in the great majority of fevers the hot skin is at the same time dry; and we shall be the more disposed, with Leyden, to regard this condition as a cause of the rise of bodily temperature, since, as already remarked, the reappearance of the secretion coincides with the reduction of bodily heat, and is profuse in proportion to the rapidity of the fall of temperature.

Still it will be well to avoid overestimating the influence of the reduced perspiration and of the suppression of the sweat secretion on the bodily heat of fever patients. The fact just mentioned, that profuse sweating is present in many febrile diseases, is enough to prove at least that the febrile rise of temperature does not depend on its non-occurrence. Further, that the connection between secretion of sweat and decline of temperature in fever is not a simple one, is taught by the fact that in the crisis the fall of temperature begins before sweating commences. That no exclusive importance attaches to the absence of the secretion in fever, is most strikingly shown by the fact that, during the fastigium, even the most profuse sweating, whether produced artificially by the injection of pilocarpin or depending on other causes, need not necessarily exercise a recognisable influence on the body heat; it is not necessarily attended by a fall of temperature, and may even be followed by a rise. Lastly, Leyden and Fränkel have recently, with perfect justice, pointed out that were the suppression of sweating of such prime importance in fever, it would follow that animals which, owing to imperfect development of the sweat-glands are incapable of sweating, like the dog and rabbit, could not possibly develop fever; which is clearly opposed to actual facts. From all this it may be inferred that the causal connection between the diminished evaporation of water and the elevation of temperature is certainly not a general or unlimited one; and if both so frequently coincide, while the fall of temperature no less often goes hand in hand with increased secretion of sweat, still it is open to discussion whether both are not co-effects of the same cause, namely of certain conditions and events connected with *the entire vascular apparatus of the skin.*

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* Leyden, 'D. A. f. klin. Med.,' v, p. 271.

† Luchsinger, 'Pflüg. A.,' xiv, p. 369.

That the *cutaneous circulation* in fever is peculiarly situated, must always have been apparent. We need only refer to the *fever-chill,* in which the arterial anæmia, *i. e.* the abnormal contraction of the arteries of the skin, will be recognised by every one at the first hasty glance. This condition does not, it is true, persist after the chill is over, but on the contrary generally gives place during the fastigium to a marked redness, *i. e.* to an increased fulness and dilatation of the cutaneous vessels. Yet at this time also signs are not wanting which point unmistakably to an abnormal state of the cutaneous vessels and of their innervation. The recently mentioned *instability* of the bodily heat in fever patients is itself evidence of this. If in fever the temperature at once rises considerably after slight mental excitement or trifling muscular exertion, this is indeed most plausibly explained by a sudden reduction of the loss of heat, yet it is open to other interpretation; the circumstance, however, that a short and trifling exposure to cold gives rise in a fever patient to a violent rigor and causes a striking fall of temperature can hardly be regarded as anything but a proof of faulty regulation on the part of the cutaneous vessels. This defective power of regulation in presence of changes of the surrounding temperature has long attracted the attention of the physician and the experimenter. Senator* found himself obliged to use warmer water for the calorimeter in the case of dogs with fever than in the non-febrile state, since the febrile animals were otherwise unable to maintain their temperature, and became cooled in the calorimeter. Naunyn and Dubczcanski† found, further, that the bodily heat of small animals in fever was very seriously disturbed by variations of external temperature which had no influence in a non-febrile healthy condition; the bodily heat of rabbits and guinea-pigs in fever was raised on exposure to external temperatures of 24°—30°, and was lowered, in spite of the fever, in air at 15°—18°. Lastly, the entire modern therapeutics of fever by cooling is based essentially upon the altered regulation of the patients. For the first physicians who systematically employed cold bathing in fever, in seeking to account for the effectiveness of this treatment,‡ came to the conclusion that the baths act differently on fever patients and on healthy persons; the cooling thus brought about is in the former essentially *greater and in particular more persistent* than in the latter.

Moreover, we have evidence of a very different kind that the state of the cutaneous vessels in fever is decidedly abnormal. I remind you above all of Heidenhain's experiments on the influence exerted by the vaso-motor system of nerves on the temperature of the body.* He has determined, you are aware, that direct or reflex stimulation of the vaso-motor centre in healthy animals causes an increase in the supply of blood to the skin, and as the result a greater loss of heat and lowering of the internal temperature. On similarly irritating the vaso-motor centre in dogs in whom fever had been set up—also whose temperature had been raised by poisoning with strychnine—*no diminution of bodily heat occurred;* no effect was produced, or an opposite result ensued, *because the amount of blood flowing through the cutaneous vessels,* as proved by the fall of superficial temperature, *was diminished,* and not increased; instead of an augmentation of heat-loss, the loss was reduced in the dogs in which fever had been set up. Here must be mentioned, further, a peculiar phenomenon which may often be observed in fever patients with a reddened skin,† namely the appearance of *an intense pallor on slight cutaneous irritation, e. g.* gentle stroking with the finger-nail, a pallor which starting from the spot irritated extends on every side till it has reached several times its original size; the skin begins to grow pale about half a minute after the stroking, and the paleness lasts perhaps four minutes, when it slowly disappears. A fact recently discovered in Leyden's‡ clinic also deserves notice, namely the slow absorption of soluble materials applied subcutaneously; while iodide of potassium usually appears much more rapidly in the urine when injected beneath the skin than when administered by the stomach, the opposite is the case during the height of a fever.

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* Senator, 'Untersuchungen,' pp. 11, 151.

† v. Dubczcanski u. Naunyn, 'A. f. experim. Patholog.,' i, p. 181. D. Finkler met with similar experiences.

‡ Cf. *e. g.* Jürgensen, 'D. A. f. klin. Med.,' iv, p. 323.

While it is evident from these facts that the cutaneous vessels behave differently in fever and in health, the nature of the disturbance does not so certainly appear. True, the pallor following slight irritations can hardly be regarded as anything but a sign of *increased irritability,* and it was in this sense also that Heidenhain originally explained his experiments. At that time, however, the vaso-dilators or, as Heidenhain has called them, the inhibitory nerves of the cutaneous vessels, were not yet known; and after their discoverer had pointed out* that the increase of the blood-stream through the skin, which in healthy animals ensues on irritating the vaso-motor centre, is essentially dependent on excitation of the inhibitory nerves, and is therefore active, the cause of the opposite condition of the cutaneous circulation in fever was more recently sought by Leyden and Fraenkel in *a deficient irritability of the dilators;* in fever the vessels are less capable of active dilatation than in health. Consequently they believe that the marked and persistent cooling of fever patients after cold baths or cold douches may be explained by the exquisitely stimulating effects exerted by cold on the cerebral system and its centres: in consequence of this reflex stimulation of the centre for the inhibitory nerves of the cutaneous vessels, these vessels dilate and receive a larger amount of blood, so that for a time the regulation and therefore the bodily heat are approximately normal, till the stimulating effect of the cold passes off and the imperfect regulation, *i. e.* the high fever, is re-established. Naunyn,† owing to the similar behaviour towards external temperatures of his febrile animals and of dogs with divided cervical cords, also regards it as most probable that in fever the nerve-centres which preside over the heat-regulation in healthy individuals are paralysed or at any rate less excitable; but in this connection you will bear in mind the various doubts to which I gave expression when dealing with laceration and division of the cervical cord (vol. iii, p. 1343) as regards the conclusions which have been drawn therefrom.

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* Heidenhain, 'Pflüg. A.,' iii, p. 504; v, p. 77.

† Bäumler, 'Med. Centralbl.,' 1873, p. 179.

‡ Leyden, 'Med. Centralbl.,' 1878, p. 708.

It would obviously not be difficult to explain most of the facts referred to in different ways,—clear evidence that the data are insufficient to afford a positive insight into the relations. Under these circumstances a very reasonable desire arose, to obtain certain results by employing more direct methods in investigating the cutaneous vessels and the blood-stream through them in fever. With this object in view, Senator‡ had recourse to direct observation of the cutaneous vessels of the ear in animals, more especially rabbits, affected

* Ostroumoff, 'Pflüg. A.,' xii, p. 276.

† v. Dubczcanski u. Naunyn, 'A. f. experim. Patholog.,' i, p. 181.

‡ Senator, 'Med. Centralbl.,' 1873, p. 85; 'Untersuchungen,' p. 153.

with fever. In this way he at once convinced himself that these vessels do not persistently remain in one unvarying state, whether of dilatation or narrowing, but carry out their well-known rhythmical contractions and relaxations, though in *exaggerated* fashion as compared with the normal. He observed the vessels undergoing extreme contraction, so that the ear grew perfectly pale and cold, and a short time afterwards saw the blood forcibly shooting into the extremely dilated arteries, with the result that the entire ear immediately became injected even to the finest vascular ramifications; he also got the impression that the alterations of the flow were not only more striking but also more persistent during each phase than in healthy non-febrile rabbits. Yet though these observations seem very positive, every one, who has had patience enough to keep the rhythmical pulsations of the ear vessels long under observation in a large number of rabbits, knows how great are the individual differences both as regards their intensity and succession, and how deceptive is consequently the attempt to come to any conclusion from quantitative differences in these pulsations alone. Hence more far-reaching importance appears to me to attach to *the measurements of the temperature of the skin in fever*, which during the last ten years have been carried out in large numbers by several writers* in a great variety of diseases. All these measurements, whether effected by thermo-electric means or by a thermometer placed between the toes, agree in proving that *the temperature of the skin presents much greater variations* at the height of a fever than are ever observed in healthy persons. Symmetrical portions of the skin, such as corresponding clefts of the toes on either side, very frequently exhibit different degrees of heat; and not only so, but when the temperature changes, the alteration does not always take place in the same direction in both. Further, as regards the relation of the cutaneous to the internal temperature, Schülein claims to have found that in some diseases, like pneumonia, measles, and scarlet fever, the temperature of the skin always conforms to and moves with that of the axilla, while in the great majority of febrile diseases such conformity does not exist. Yet the other writers on this subject have not been able to confirm this relation in the diseases just named, and it may therefore be said generally that in fever the course of the internal temperature need not run parallel to that of the skin. While the internal temperature persistently remains at a very considerable elevation, the skin may at the same time present an alternation of really high values with conspicuously low ones, so that, *e. g.* in a patient in whom the fluctuations of axillary temperature amount to little more than one or at most two degrees, the heat of the skin may vary as much as 16°. During the fever-chill the fall of the cutaneous, evidently coincides with the rise of the internal, temperature; in the sweating stage both temperatures are approximately the same, and indeed the skin may be warmer than the axilla. Lastly, the results of calorimetric investigations may also be utilised in estimating the condition of the cutaneous arteries, and I remind you therefore of a characteristic feature which appears very prominently from Leyden's estimations, namely *the striking variations in the amount of heat-loss* without any analogous alterations of bodily temperature (cf. vol. iii, p. 1377).

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* L. Jacobson, 'Virch. A.,' lxv, p. 520; Schülein, ibid., lxvi, p. 109; Wegscheider, ibid., lxix, p. 172; Schuck, 'Ueber d. Schwankungen d. Hauttemperatur bei Fieberkrankh.,' Inaug.-Dissert., Berlin, 1877; Niesse, 'Ueber d. Verhältniss d. peripheren Temperatur zur centralen im Schweissstadium d. Menschen,' Inaug.-Dissert., Berlin, 1877.

The agreement, you perceive, could not be more complete; measurement of the cutaneous temperature, determination of the loss of heat, and the direct observations of Senator all teach *that during the height of a fever, the state of fulness of the cutaneous vessels and the blood-stream through them are liable to continual variations* of much greater intensity than in non-febrile, healthy individuals. After periods of strong arterial hyperæmia, during which the skin is warm and gives off much heat, there occur intervals of marked anæmia with cooler skin and slighter heat-loss, and when these have lasted for a time they are again interrupted by periods of congestion. No sort of regularity in the duration or sequence of these variations has hitherto been recognised, and it is unlikely that such regularity exists, if for no other reason, because the state of fulness of the cutaneous vessels in the various areas of the body is usually very unequal; while the hands are pale, the skin of the trunk may be markedly red, and a thermometer placed between the toes may show much higher values on one side than on the other. To enable us to satisfactorily deduce these varying conditions from alterations in the state of irritability of the vessel-nerves or centres which control the arteries of the skin, our knowledge as to the activity of the constrictors and dilators in fever is in my opinion insufficient; all the less, however, shall we allow ourselves to be troubled by the fact of the occurrence of fluctuations and alternations in the behaviour of the cutaneous vessels in fever, a fact which affords us the opportunity of really explaining the febrile rise of temperature. Consider in what the actual difficulty consists. Since it has been determined that the oxidative processes are abnormally augmented in fever, there can no longer be any doubt as to the source of the excess of heat. Nevertheless, we asked, how does it happen that fever patients do not get rid of the overplus of heat with the same ease and completeness as do healthy persons despite a much more vigorous heat-production? and this question becomes all the more pressing since it has been proved by calorimetric means that in fever the increase of production is in fact accompanied *pari passu* by an increase of loss. We now know why the heat lost by the skin does not suffice to remove the entire excess of heat; the cause consists in this, *that the conditions which favour the abundant loss of heat are not continuously present so long as the abnormally abundant heat-production lasts.* Did the cutaneous vessels continue dilated and supplied by a copious and rapid blood-stream, it is at least highly probable that the bodily temperature would not rise at all despite the increased production of heat. It is not so, however, in reality. For probably at no time during fever are all the arteries of the surface congested; rather the vessels over more or less large areas are always in a state of marked contraction: those febrile diseases which, owing to the short pyrogenetic stage, begin with a rigor, are initiated by a wide-spread tetanic contraction of the cutaneous vessels; during the fastigium, the intensity, duration, and extent of this contraction are usually less, yet, as stated, it is never absent; only in the stage of defervescence, especially when running its course rapidly, it may fail to be observed. Narrowing of the arteries, however, involves a *diminution of heat-loss*, which is due to reduction of the perspiration as well as to limitation of the yield by conduction and radiation. At the same time it is not necessary that the amount of heat-loss should fall below the normal standard—which, in fact, it rarely does in fever: a relative reduction—relative as compared with the increase of production—suffices to explain the increase of bodily temperature. In the physiological organism also, a certain amount of heat is at all times produced by the oxidative processes taking place within it; while, on the other hand, the arteries of the skin, like those of all other organs, undergo constant variations of calibre, by whose prompt working, the one into the other, provision is made that the loss of heat shall always conform to the production, and in this way the temperature is maintained approximately constant. If, on the other hand, an exciter of fever has acted upon an individual, there takes place a growth of the activity and amount of the oxidative processes and consequently of heat-production, while the variations in the calibre of the cutaneous arteries are considerably augmented, with the general effect, it is true, of causing an abnormally great loss of heat, yet—in consequence, it would appear, of the more marked increase of the periods of constriction—*not in a measure corresponding with the growth of heat-production*: the necessary result is an elevation of the bodily temperature. Before concluding this part of the subject, I may say a few words as to the historical development of our present doctrine of fever. In the progress of science, the fundamental proposition of Traube's theory—that heat-production continues normal, while the loss of heat is reduced by persistent tetanic contraction of the cutaneous arteries—has been absolutely overthrown. Nevertheless, after having followed my exposition so far, you will certainly admit that I was perfectly justified in calling the publication of Traube's theory an event of the greatest importance, and fraught with weighty results as regards the entire doctrine of fever; for it not only provoked a number of valuable and fruitful researches, by which our knowledge of the fever process has been greatly furthered, but it had above all the merit of having first given prominence to the point which alone allows of an understanding of fever, namely *the abnormal behaviour of the heat-loss.*

From the standpoint now arrived at, it will be advisable to examine fever in all the details of its manifestation. By adopting this course we shall most fully test the correctness of our statements; for not only is it necessary that we should succeed in explaining all phases of the febrile alteration of temperature, but if it be true that the increase of bodily heat is the essential fundamental phenomenon of fever, it must be possible to deduce all the manifold symptoms, presented by the different systems of the body, from the disturbances which we found to take place in connection with the factors regulating the temperature of the organism. Perhaps it may also be possible in this way to get a more accurate acquaintance with the morbid metabolic processes, whose result we recognised in the increase of heat-production. For although it is generally speaking more than probable that the nervous system controls and regulates the factors of heat-production no less than of heat-loss, it is indispensable to a positive insight into the conditions of fever that we should know the organs and tissues in which the increase of the oxidative processes, probably set up by the agency of the nervous system, take place.

The rise of temperature in the *initial stage of fever* may be explained without difficulty. For it has here been demonstrated almost more strikingly than in any of the later stages that, on the one hand, the production of heat is increased, and that, on the other hand, owing to the great irritability of the vaso-constrictors of the skin, the loss of heat is at most scarcely greater, and is not uncommonly less than normal. The importance possessed by the state of the cutaneous arteries as regards the febrile increase of bodily heat nowhere appears so glaringly as in the fevers which have a short pyrogenic stage, where, as more than once emphasised, the occurrence of a tetanic contraction of the arteries over extensive cutaneous areas is absolutely characteristic. But not only is the rapid rise of bodily temperature rendered intelligible by the considerable limitation of heat-loss so brought about; the subjective sensation of cold is also explained by it. It is undeniably somewhat extraordinary in itself that a person should have a marked sensation of cold, and go through involuntary muscular movements at a time when his bodily heat is increasing by several degrees. Yet the riddle is solved very simply, I think, on considering the conditions on which our sensations of temperature depend.* For the apparatus supplying us with such sensations, *i. e.* the terminations of particular nerves in the skin, are not so contrived that we can recognise a definite external temperature as such; *the determining element in our sensations of temperature is the temperature of the thermal apparatus itself.* So long as its temperature remains constant we have no sensations either of heat or cold, while we become sensible of each increase of its temperature as heat and of each decrease as cold. Which of the two occurs, depends self-evidently on the relation of heat-supply to heat-loss; the equilibrium between these involves constancy, and every disturbance of equilibrium, according to its nature, an increase or decrease of the temperature of the apparatus. But while the sensation of cold in consequence of an increased loss of heat is a daily and therefore familiar experience, diminution of heat-supply to the thermal apparatus is a less ordinary, but none the less effective, means of reducing the temperature of the latter, and of thus giving rise to the sensation of cold. This, however, is effected to a marked extent by the contraction of the small cutaneous arteries; for though the loss of heat is thereby reduced, it is not, for obvious reasons, diminished so greatly and above all so rapidly as is the heat-supply, which depends in by far the greater part on the blood-stream. The more energetic, rapid, and extensive the arterial contraction, the more is the equilibrium between supply and loss of heat disturbed to the disadvantage of the former, and the more pronounced and severe does the sensation of cold, the chill, become. The fever-chill you see is simply a result of the acute tetanic contraction of the cutaneous arteries, and you will therefore not be surprised to hear that all the symptoms of this chill may sometimes occur independently of fever and in the absence of the considerable rise of bodily heat. Many persons, the vaso-motors of whose skin are beyond doubt easily excited, get a regular rigor as the result of ordinary intestinal colic or even the passage of a catheter, and this is only and solely the effect of a wide-spread reflex tetanus of the cutaneous arteries, and has nothing to do with fever. On the other hand, you will readily understand why it is that if the initial stage be protracted, the fever-chill is slight or completely absent. In such fevers there is no tetanic contraction of the arteries extending in the shortest time over large portions of the skin; the narrowing of the cutaneous vessels develops slowly and is liable to continual fluctuations, and never becomes so pronounced as in fevers with a short pyrogenic stage. There is therefore at no time a rapid disturbance of the temperature of the thermal apparatus, and nothing to originate a marked sensation of cold.

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* Cf. Hering, 'Wien. akad. Sitzungsber.,' Abth. 3, lxxv, p. 101, 1877.

But even in fevers ushered in by a rigor, the tetanic contraction of extensive cutaneous arterial areas does not last longer than the initial stage, and gradually declines as the *fastigium* is approached. The means of access to the apparatus which receives sensations of temperature is thus again opened up to the blood, and to blood, moreover, which is heated considerably above the normal; the necessary result is that the patient *now experiences a marked sensation of heat.* The increase of heat-production lasts during the entire fastigium, while at the same time the loss of heat is augmented as compared with the normal, though not in proportion to the production. That this disproportion depends on a pathological behaviour of the cutaneous circulation is established by most adequate proofs; yet the facts hitherto acquired are insufficient to enable us to certainly decide whether deficient irritability of the vaso-dilators, with consequent inadequate dilatation of the cutaneous arteries, or increased irritability of the constrictors plays the greater part in it. True, we have usually to deal only with a temporary and moderate constriction of circumscribed arterial areas, and it happens only exceptionally in the fastigium that the arteries of extensive regions of the skin are thrown into strong tetanic contraction. Such tetanic contraction takes place when a fever patient is attacked during the fastigium by a more or less violent rigor —an event which, as you know, occasionally occurs in all varieties of febrile disease, no matter what their course.

Moreover, the rigor in this instance resembles that of the initial stage in that a rapid and not inconsiderable rise of bodily heat takes place during it,—in part certainly an effect of the wide-spread contraction of the arteries, although it is unquestionable that heat-production simultaneously receives a fresh impulse. As to the means whereby it is brought about that at the height of the fever the secretion of sweat is as a rule suppressed, though blood of high temperature bathes the centres as well as the terminations of the sweat-nerves and the glands, on this subject, as already stated, we possess no accurate information.

In the *period of defervescence,* lastly, the normal condition is again re-established. Heat-production is reduced to its normal standard, and the conditions of heat-loss again conform to the laws prevailing in the physiological organism. This latter change is rendered possible by an alteration of the cutaneous circulation such as occurs in a healthy person who from any cause has produced an excessive quantity of heat. Henceforward neither general nor circumscribed arterial contraction is present; the arteries become wide owing to the vigorous action of the dilators, and a strong and ample blood-stream flows through the vessels of the skin. The result as regards the heat of the body will naturally be striking in proportion to the rapidity with which these changes set in. The loss of heat may in fact under these circumstances considerably overbalance heat-production, so that within a few hours the temperature falls by several degrees. When this happens, there is also present an abundant, often profuse, *secretion of sweat*—evidence that the factor arresting this secretion has disappeared, the sweat-glands now actively reacting to the increased heat-production just as in a healthy person. The abundant secretion of sweat is accordingly a *consequence of the restoration of the normal relations,* though at the same time one of the means of which the organism avails itself to accelerate the cooling of the body. For while we were formerly able to determine that even a very profuse secretion of sweat exerts no influence on the bodily heat so long as the conditions persist on which the faulty production and loss of heat depend, it cannot be doubted that, when these conditions are removed, sweating is calculated, just as in health, to lower the temperature of the body. True, it is only in a limited number of diseases that the decline of temperature follows so suddenly or *critically;* yet it is unnecessary to explain more minutely that the slow decline by *lysis* depends on *a slow and far from continuous* restoration of the normal conditions of heat-production and of the normal relations of the cutaneous vessels.

While, accordingly, our interpretation of the process of fever allows of an unforced explanation of the three chief periods of every febrile disease, it no less admits of our estimating certain peculiarities of the febrile temperature to which I have already repeatedly referred, namely its many *fluctuations* during the course of the fever, the want of uniformity and the great *instability* of the bodily heat. The variations of temperature occurring during a single day are not, as you know, peculiar to fever; such variations are also present in health, so that it would be surprising were they completely absent during the fastigium. The peculiarity in fever is simply that the fluctuations in question are usually decidedly greater than in a physiological condition; it is nothing uncommon for the morning and evening temperatures to differ by more than 1 or even 1·5°. Our interpretation, however, offers, as I think, a sufficient clue to the explanation of this circumstance. We shall hardly meet with opposition, if we seek the cause of the normal diurnal fluctuations in the unequal intensity of the heat-producing processes, which would probably influence the bodily heat to a still greater extent, did not the heat-loss vary in a corresponding direction. But because this means of compensation does not act with the same certainty and promptitude in fever as in health, any variations of heat-production tell more conspicuously on the temperature of the body, *i. e. the fluctuations become more considerable.* I have also repeatedly pointed out in how great a degree the irregular behaviour of the cutaneous circulation must favour the tendency to change and the marked instability of the bodily heat. We do not meet with any real difficulty till we attempt to explain the occurrence, not simply of fluctuations of the fever-temperature, but of alternations of periods of increased bodily heat with others during which the temperature is normal,—to explain, that is, fever of the *intermittent* type. A patient suffering from *intermittent fever* passes in each paroxysm through all three febrile stages, and in a day or two, according to the fever-type, finds himself perfectly well, with a temperature which, when the sweating is over, is not rarely subnormal, owing to the extreme loss of heat; in other respects too it exactly resembles that of a healthy person, till a fresh rigor introduces the next paroxysm. The condition of a patient in *relapsing fever* is essentially the same; for the principle is not affected by the facts that the fastigium of the single paroxysm and the apyrexial interval last much longer than in intermittent fever, and that the number of attacks is always limited, in most cases amounting to not more than two or three. To render this course intelligible, it is not sufficient to point to the diurnal variations in heat-production and the irregularities of the cutaneous circulation. Yet to our knowledge of relapsing fever it is due that we are no longer obliged to regard the intermittent type as a remarkable and incomprehensible fact. We have become acquainted with the actual cause of relapsing fever in those organisms which are called after their discoverer *spirillum* or *spirochæte Obermeieri.* These spirilla are not only the cause of the disease but of the fever, as is most evidently proved by their presence in the blood during the paroxysm, their disappearance from it shortly before the fall of temperature, their complete absence during the period of apyrexia, and their reappearance a few hours before the next attack. The intermittency is here obviously most closely connected with the life history of the spirillum, and it is certainly not too venturesome, having regard to the equal duration of the apyrexia in all cases, to pronounce the spirilla of the subsequent paroxysm to be the second generation or descendants of those present in the preceding one: when the spirilla lose their capacity for propagation or development in the body of the patient, the disease is at an end. In intermittent fever very similar conditions prevail, although we have not yet succeeded in discovering well-marked organisms which during the paroxysm circulate in the blood or tissue-juices of the body, and disappear in the stage of apyrexia. But if we are correct, the disease is due to the invasion, as a rule a single one, by certain parasitic organisms; and the fever is not continued simply because the schizomycetes exciting it are not continuously present in the blood and juices of the body. Rather, after they have for a longer or shorter time—during the paroxysm—circulated therein, they either perish or retire to a locality in which they are innocuous, whereupon the fever terminates; a fresh rise of temperature not taking place till the schizomycetes themselves or more probably their descendants penetrate anew into the juice-stream of the body. *The intermittent character,* you perceive, *is a peculiarity of the disease, but not of the fever* as such; on the contrary, each paroxysm constitutes a complete fever with its initial period, fastigium, and stage of defervescence. Should you, however, as against this explanation recall the febrile diseases marked by the occurrence of irregular rigors, in particular the *pyæmic* and *septic,* in which also intervals of complete apyrexia occur between the periods of fever, it must be confessed that the intermittency cannot here depend on a regular succession of generations of parasites; nevertheless, I think the determining element in this case also is the *irregular presence of the cause exciting the fever.* The organism always reacts with a rigor and febrile rise of temperature, when infective masses reach the circulation from the focus of disease, and the fever lasts till the body gains the upper hand, when the infective material is excreted or destroyed; there is then a cessation of the fever, which lights up afresh on a renewed invasion by infective materials. The continuous feature is the presence of a pyæmic or septic infected wound, of an abscess or other focus of disease; the fever itself is not continuous because the presence of the foci does not alone suffice to excite fever; the constituents of the foci must first enter the juices of the body. It is far from necessary that this should occur continuously; whether and when it takes place will depend on a great variety of conditions.

If, leaving the disturbances of bodily heat and of the sensations of temperature, we now turn to the other phenomena observed in fever, we find that the symptoms connected with the circulatory apparatus occupy the chief place in point of constancy and importance. With these symptoms you are already essentially acquainted. For I have repeatedly pointed out in the first section of these lectures that *in fever the frequency of the pulse is regularly, and sometimes very considerably, increased.* It was first shown by physiologists that the frog's heart contracts more frequently in proportion as the temperature is raised, and from this it was a simple inference that the febrile rise of temperature also accelerates the pulse-rate. Liebermeister,* by simultaneously recording the temperature and the pulse in a great number of adult fever patients, has succeeded in deducing the law that, despite all variations in individual cases, the arithmetic mean for the pulse-frequency increases in exact conformity to the bodily heat, so that a rise of temperature of 1° corresponds on the average to an acceleration of the pulse by eight beats in the minute. While, then, the pulse-rate may in some degree serve as a measure of the height of the fever, we have yet good grounds for not now attaching such importance to this factor as the older physicians of necessity did before the introduction of the thermometer. For we know that the contractions of the heart depend on a number of other factors besides the heat of the blood, and that the effect of the latter may in certain circumstances be considerably modified or even concealed. Of these other factors, the most important is the state of excitation of the vagus, and you will therefore not be surprised to hear that in basilar meningitis the frequency of the pulse is even less than normal, despite the high fever. Yet even in the absence of an exudation in immediate contact with the vagus, its centre may be very variously excited during the course of a fever, and that by the arterial pressure, the height of which exerts a determining influence on the tone of the centre for the vagus.

The state of the *blood-pressure* in fever cannot be inferred from the relations already discussed. It would more particularly be erroneous to conclude from the contraction of the cutaneous arteries, which may in some periods of the fever be so marked and wide-spread, that the arterial pressure must be considerably raised. For if, as there is much reason for believing, a dilatation of some of the arteries of the internal organs coincides with the contraction of those of the skin, the blood-pressure need not undergo any alteration; indeed, it may suffer a fall, despite the increased resistance in the cutaneous arteries. There is still a want of adequate measurements of the blood-pressure in fever. As regards the only form which we can voluntarily produce in animals, the septic as the result of injecting pus, I formerly told you (vol. i, p. 91) that the mean arterial pressure is, as a rule, *low*. Yet there are exceptions even to this, and certainly we have no right to refer this lowness to the rise of temperature, since, as you will remember, artificial warming of a dog usually causes the pressure to increase, provided the temperature does not reach enormous values. In man also, in so far as may be inferred from the character of the pulse and other general indications, the condition of the *blood-pressure* in fever is very far from being always the same. If a previously healthy and robust individual is attacked by an acute febrile disease, *e. g.* pleuro-pneumonia or erysipelas, the pulse is usually large, full, and of considerable tension; and it usually presents the same characters during the first few days of a more prolonged fever, *e. g.* enteric. In some other febrile diseases, in particular the septic and pyæmic, the patient, on the contrary, has from the outset a soft, yielding and compressible pulse, and this is also the rule in the later stages of every protracted fever. A full and tense pulse is in general characteristic of those fevers which were termed by older writers *sthenic*, while the soft and empty artery is a peculiarity of so-called *asthenic* or *adynamic* fever. At any rate this nomenclature, at present almost fallen out of use, is less important than is a knowledge of the causes giving rise to these conspicuous differences. One fact appears to me to be peculiarly significant,—that the same febrile disease which at the outset presented a distinctly sthenic character, shows after a time a no less markedly asthenic type; for from this it conclusively follows, I think, that the alteration is due, not to the particular disease or its cause, but solely to the *long duration of the febrile rise of temperature*. Why it is, however, that persistent rise of temperature lowers the arterial tension, or, in other words, causes a *fall of the arterial blood-pressure*, will at once be clear to you on calling to mind the pernicious effect exerted on the heart by excessive increase of the bodily heat. The effect which is rapidly produced by too strongly overheating the blood is called forth by a less extreme degree of heat when prolonged; the contractile energy and functional power of the heart decline. Even when from the onset of the fever the arterial pressure has been low, this is due simply to a *diminution of the motive force of the heart:* a diminution, it is true, which in this case depends, not on the increase of temperature, but on the nature of the particular disease, or rather its cause. It is certain, moreover, that individual peculiarities here participate to some extent, so that, for example, the energy of the heart is much earlier impaired by the high temperature in feeble or anæmic persons than in the robust and previously healthy. But whatever the factor influencing the arterial pressure in fever, its sole importance, as regards the cardiac contractions, is the kind of influence exerted by it. When the arterial pressure is high, the active and persistent stimulation of the vagus-centre guards against an excessive increase of pulse-frequency; while a low pressure, even in the absence of fever, is usually accompanied by an acceleration of the heart-beats, and gives rise to a further increase of the pulse-rate when this is already augmented by a fever. With this conclusion, drawn from physiological premisses, experience at the sick bed fully accords. One of the distinctive signs of asthenic fever is the considerable frequency of the pulse, which very often has lost its relation to the elevation of temperature; and the attention of clinicians was early attracted by the fact that, at the same degree of bodily heat, the pulse is much less frequent in robust individuals than in feeble persons and patients exhausted by antecedent disease. Nor is it without just cause that good observers have always regarded it as a bad sign when a moderate rise of temperature coincides with great frequency of the pulse. For from this combination we may infer with a high degree of probability that the blood-pressure is low; low blood-pressure, however, involves, as you know, more or less profound functional disturbance of some or all the organs, while, as regards the circulation itself, it implies a retardation of the flow, a tendency to hypostatic congestion, and an undesirable overfilling of the venous system. Such circulatory disturbances are, in fact, rarely missed in the more severe and somewhat protracted fevers, and may, under certain circumstances, attain such severity as to endanger life.

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* Liebermeister, 'Handb.,' p. 464, *et seq.*

Among the most common symptoms of fever are, further, all kinds of *nervous disturbances,* whence it is apparent that the nerve-centres do not perform their functions normally in fever. It is chiefly through these disturbances—disregarding possible local affections—that the feeling of illness is first aroused in the patient, and the attention of his friends is drawn to the fact. The intensity of the symptoms varies extremely. In the milder cases, the sensorium is, it is true, unclouded, yet the patient has an undefined general *malaise;* he feels languid and depressed, his head is heavy and confused, he is at the same time irritable and restless, and his sleep is disturbed. All these phenomena are more pronounced in severer cases: the mental confusion is still greater, and the patient is indisposed for, and incapable of, intellectual exertion; consciousness begins to be obscured for a time, the patient grows more apathetic, his replies are hesitating; regular, refreshing sleep is mostly completely absent, but there is a tendency to doze, and slight delirium sometimes occurs in the half-sleeping state. In extreme cases this condition is still more aggravated; there is marked and lasting *clouding of consciousness,* while various evidences of irritation or depression testify to the abnormal state of the central nervous system. Many patients are excited and appear as if actually intoxicated, they give expression to their hallucinations in boisterous delirium, while at the same time they are extremely restless and attempt to spring out of bed or even out of the window; in children general convulsions will then probably set in. Others, on the contrary, lie in a state of profound apathy, out of which they can hardly be roused by the loudest call, and scarcely react to any sense-impression; at the same time there is quiet muttering delirium, the excrements are involuntarily evacuated, the hands move tremulously as the patient picks at the bedclothes, and the posture of the completely prostrated, unconscious individual is altogether passive and relaxed.

All these disturbances have usually been directly referred, more especially during the last two decades, to the febrile rise of temperature as their cause: the central nervous system, being supplied with blood of abnormally high temperature, is supposed as the result to perform its functions irregularly and to react to the impressions reaching it with all sorts of morbid sensations, &c. Yet it cannot, in my opinion, be asserted that this view has been proved with scientific precision and may therefore lay claim to unreserved applicability. The fact, moreover, that all these nervous disturbances are wont to be more considerable the higher the temperature, that these symptoms generally run parallel to the severity of the fever, is not sufficient of itself to secure the view against every objection, since a high fever is at the same time a sign of severe disease. Now, you will remember that the very great majority of all febrile diseases are called into existence by a noxa which has entered the body, and the effect of which is not simply the febrile rise of temperature, but a number of other functional disturbances and changes constituting in their totality the particular disease; and in this precisely lies the difficulty of distinguishing between the symptoms which are due to the fever as such and those which are the direct effects of the noxa. The nervous symptoms above described have no such specific characters, however, as to render it inconceivable that they might be the result of different kinds of noxæ. On the other hand, the strict adherents to the view of the purely febrile nature of the nervous symptoms also admit that many variations in kind and especially in degree are met with in fevers of the same intensity, and these they seek to explain by a reference to individual peculiarities in the patients. But while I am quite willing to admit the importance of idiosyncrasy, it is impossible not to see that the *nature of the disease* exerts an essential influence on the character of the nervous symptoms. Despite the frequently extreme elevation of temperature during the paroxysm of relapsing fever, we hardly ever meet with those evidences of profound depression which are rarely absent in enteric and septic fevers, even when the bodily heat is much slighter, and which may in many patients be very pronounced although their temperature may never considerably exceed the normal.* To this must be added the interesting fact established by Genzmer and Volkmann† that in wounds treated by Lister's method and in ordinary simple fractures, though there may be a very considerable rise of temperature (cf. vol. iii, p. 1365), *nervous symptoms may be completely absent.* Such patients go about cheerfully with temperatures of 39° and 40°, amuse themselves, are chatty and bright, exactly like perfectly healthy persons. Whether you will, with Volkmann, term such fever *aseptic*, in direct contrast to ordinary wound-fever, I shall leave to your own judgments; its occurrence at any rate proves that there is no such close causal connection between rise of temperature and nervous symptoms as Liebermeister‡ and others have declared to exist.

Nevertheless, I should be sorry to mislead you into depreciating the importance of the rise of temperature to the functions of the central nervous system. For though a considerable number of the nervous symptoms observed in febrile diseases must be referred to the cause of disease, this by no means implies that it is a matter of indifference as regards the nervous system whether the blood supplied it has the normal or an abnormally high temperature. In the first place, the *absolute elevation* of the temperature is certainly material. The bodily heat of Volkmann's patients mostly varied between 39° and 40°, the latter limit being only exceptionally exceeded; hence it is questionable whether the sensorium would have remained equally unaffected had the aseptic fever attained the really high values of 41°, 41·5° or more. When these temperatures are reached in the paroxysm of relapsing fever, the patients exhibit at any rate sleeplessness, restlessness, and dulling of the sensorium, though when the fever is moderate the central nervous system is only very slightly affected; and in general there is probably no internal febrile disease, where the periods during which those highest degrees of temperature are present are not marked by more or less severe nervous symptoms. In the second place, much certainly depends on the *duration* of the febrile rise of temperature. The paroxysm of relapsing fever terminates after four or five days, and the aseptic fever also rarely lasts longer than a week: the most intense nervous symptoms, however, and especially the evidences of depression, are observed precisely in patients in whom the fever has continued for a considerable number of days. True, in these cases the arterial blood-pressure is invariably low, so that the functions of the brain must also necessarily suffer in consequence; and if the sensorium of a typhoid patient becomes clearer after a cold bath, it is hard to say how much of this effect should be attributed to the cooling and how much to the improvement in the circulation and rise of blood-pressure, brought about by the bath. The entire question is obviously not yet ripe for decision, and is certainly more complicated than at first appears; yet it is in any case established that whatever nervous symptoms may set in during a fever, they are certainly secondary in their nature.

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* Cf. Fraentzel, 'Ztschr. f. klin. Med.,' ii, Hft. 2.

† Genzmer und Volkmann, 'Volkmann's Vortr.,' No. 121, 1877.

‡ Liebermeister, 'Deutsch. A. f. klin. Med.,' i, p. 543, *et seq.*; 'Handb.' p. 481, *et seq.*

The same thing applies to the phenomena observed in connection with the *muscular apparatus* of fever patients. In almost every somewhat severe fever, the patients complain of weariness and want of energy together with marked *muscular feebleness;* and this is not simply a subjective sensation, for the functional power of the muscles is in fact so reduced that the arm of a patient, who wishes to convey a glass to his mouth, can only be extended with difficulty and exhibits marked tremors on movement; we also recently mentioned loss of muscular power as a cause of the passive posture of fever patients. It is something very common, moreover, in all possible febrile diseases, even when *per se* they have no connection with the muscular apparatus, to find *muscular pains,* which are sometimes very wide-spread and may be so severe that the patient can hardly avoid crying out at every touch. To what extent these symptoms are referable to an abnormal condition of the central or peripheral innervation, is scarcely to be made out; yet one is tempted in the case of the muscles to admit the idea of the occurrence of certain *chemical changes* of their contractile substance, perhaps a commencing coagulation of the muscle-fibres. I have, moreover, made you acquainted on a former occasion (vol. ii, p. 684, *et seq.*) with some muscular changes which are calculated to favour this idea, namely *parenchymatous* and *waxy degenerations*. In treating of the former, we considered the possibility of the coagulation of a fluid normal or modified albuminous body; while, as regards the latter, it seemed to us most probable that it is the expression of an irregular coagulation of the muscle-fibres which for some cause or other have perished *intra vitam*. As regards the actual cause of these alterations, we are obliged to leave it doubtful how much must be ascribed to the rise of temperature and how much to the agent exciting the particular disease.

That the *digestive apparatus* is liable to various disturbances in febrile diseases, you already know. I was in a position to tell you that, under the influence of the febrile rise of temperature, all the digestive juices are affected, some of them being produced in smaller quantity, while the activity of others is reduced. This being so, I need not refer to the faulty manner in which the peristaltic movements of the intestines take place in fever, in order to render it intelligible to you that digestion will be more or less seriously deranged. To this the *anorexia* of fever patients is in a great measure attributable, although it is also due in part to the dryness of the tongue and buccal mucous membrane, to which reference was also made, and to which too the unpleasant taste and clamminess of the mouth are to be referred. The dryness of the tongue is at any rate the chief cause of the increased *thirst* of fever patients, which cannot be attributed to a supposed concentration of the juices and tissues of the body. Where the tongue is moist, as in Volkmann's patients suffering from aseptic fever, the thirst is only very slightly increased. True, these individuals also exhibited no falling off of appetite—a fact which again suggests the doubt whether it is really the rise of temperature alone that so seriously impairs the functional power of the digestive apparatus.

We have also already discussed the principal symptoms connected with the respiratory apparatus in fever. Chief among them is the *increased frequency of the respirations*. Every patient, of whatever age and sex, breathes more frequently in fever than in a non-febrile condition. That the more rapid breathing is a direct result of the rise of temperature of the blood, is at present accurately known as the result of the artificial over-heating of animals, and more especially of the experiments of Fick and Goldstein (vol. iii, p. 1095). But as regards fever also, no unprejudiced observer can have doubted the existence of the connection. In equally robust persons of the same age the respiratory frequency runs in general parallel to the temperature curve; and in different diseases, and different periods of the same disease, the patients breathe the more rapidly the greater the bodily heat; indeed, the number of respirations increases and decreases with the diurnal variations of temperature. Moreover, this applies not merely to those febrile diseases which have nothing to do with the respiratory apparatus, but also, for example, to pneumonia; the rapid breathing terminates with the crisis, although the extent of the infiltration is as yet unreduced. This obviously does not tell against the possibility that one or other of the many factors with which we became acquainted when studying the pathology of respiration may in fever also exert its influence on the number and mode of the respirations. But we are here interested merely in the effect of the fever as such, and this, as has been said, is invariably to increase the number of respirations. At the same time the breathing usually becomes deeper, at any rate in robust individuals and in acute diseases of short duration as well as in the early period of more protracted fevers; so much is this the case that the amount of air respired by such a patient is not inconsiderably increased as compared with the normal. The utility of this increase will at once be apparent on remembering that the production of carbonic acid is abnormally large in fever. True, when the pyrexia has lasted long, and marked muscular feebleness has occurred, an increase of the depth of the respiratory movements ceases to be possible; instead of this, we have an abnormal shallowness of the breathing which, as you know, must give rise to a further increase of frequency, whereby the interchange of the gases of the blood will not, it is true, be so greatly facilitated as by the previous less numerous but deeper respirations of the early period of the fever.

Lastly, we may, after our former discussions, briefly dismiss the febrile alterations of the *urinary secretion*. The amount of urine passed in fever is *reduced* throughout, sometimes even to half the normal. That this diminution is due partly to the smaller amount of nourishment taken and partly to the increased loss of water in other directions, you already know. The limitation of the water-supply from without is not compensated in the fever patient by the increased feeling of thirst; and as regards the loss of water by other channels, its increase is contributed to by the lungs, owing to the more frequent respirations and greater heat of the expired air, and by the skin, by means of the augmented perspiration: moreover, during the periods of profuse sweating, the reduction of the urinary secretion is still more striking. In prolonged fever, when the energy of the heart has already suffered, another factor also contributes to diminish the secretion of urine, namely, the *fall of arterial pressure*, which for the rest may set in very early in some febrile diseases, *e. g.* the septic processes. In patients suffering from Volkmann's aseptic fever, however, there is no noteworthy diminution of the urine, because, far from labouring under anorexia, they take an abundance of food, while their arterial pressure is maintained constant at the normal elevation. It is not so easy, on the other hand, to explain the absence of all diminution of the excretion in short febrile paroxysms or in simple continued fevers, which are sometimes accompanied by a decided increase in the volume of the urine: for whether this condition actually depends on an augmentation of the blood-stream through the kidneys as the result of a tetanic contraction of the cutaneous arteries,* cannot be certainly determined till we have become more accurately acquainted with the state of the arteries of the internal organs during the different phases of fever than has heretofore been the case.

As regards the other characters of the urine in fever, you will remember how carefully we discussed its comparative richness in nitrogenous matters, especially in *urea*. This fact, together with the scantiness of the secretion, is, you are aware, the cause of the frequent precipitation on cooling of an abundant sediment of slightly soluble *urates;* to it is due also the *high specific gravity* of the febrile urine. The urine is concentrated although its *saline* contents are reduced below the normal, the amount of chloride of sodium present being so small that we failed to adequately explain the decrease from the ordinary factors of food-supply, loss of salts in other ways, &c. (cf. vol. iii, p. 1112). The *potash salts* alone are excreted in considerably larger quantities than in the urine of healthy persons on the same diet (cf. vol. iii, p. 1113); a fact which is worth nothing, because it indicates that, among the substances which disintegrate in the organism during fever, there must be some which are relatively rich in compounds of potash. Take in connection with this the fact that febrile urine is always high-coloured, not merely by reason of its concentration, but because the *urinary pigment* is positively increased, and it will appear a very probable conclusion at least, that in fever considerable numbers of *red blood-corpuscles* are made to disintegrate, a conclusion to which other evidence also points. How frequently, in the last place, a small quantity of albumen and a few hyaline casts are contained in the urine of fever is also known to you from our discussions on albuminuria.

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* Liebermeister, 'Handb.,' p. 494.

Standing in sharp contrast to this rich and varied group of symptoms, in which almost every organ of the body is involved, is the dearth of all characteristic *pathologico-anatomical* changes. Not that such are completely absent from the body of persons dying from a febrile disease! Some of the changes, however, like phlegmonous inflammation or a tonsillar abscess, must rather be looked upon as the cause of the fever; of the remainder, the vast majority are not, it is true, the causes, but just as little are they effects of the fever. A pneumonic infiltration, a swelling of the spleen, a diphtheria of the pharynx, do not bear to the fever any but a co-ordinate relationship; they are just as much the products of the particular exciter of disease as is the fever itself. As regards a third series of alterations, very frequently observed in protracted febrile diseases, such as bedsores, atelectases, and hypostatic congestions of the lungs, it is indeed undeniable that the persistent fever exerts an essential influence on their development, yet the connection is obviously an indirect one, and the changes are certainly not of such a kind as to admit of their being recognised as the specific effects of the fever. These, moreover, are not the changes referred to when the anatomical effects of fever are spoken of. The writers who do so have in mind, rather, certain alterations of glandular and muscular organs which are supposed to pass through certain gradations, originating in granular clouding and swelling and going on to marked fatty degeneration and disintegration. These alterations are not unknown to you; for we have minutely treated of them under the head of *cloudy swelling* or *parenchymatous degeneration* (vol. ii, p. 684), and we then discussed their hypothetical relation to febrile rise of temperature. True, we had to be satisfied with expressing ourselves very aphoristically, because we were unable to say anything definitely as to the real nature of this degeneration. We discussed the question as to whether a separation in solid form of a fluid albuminous body was concerned in the change, because the chemical reactions left no doubt that the granules in cloudy swelling are albuminous. For this reason too we felt ourselves bound to uphold the distinction between this change and true fatty degeneration, though we did not deny the possibility that fat may be separated from the albumen of the particular organs. We found fewest positive indications, however, of a causal connection between both these changes and fever. In the experiments,* carried out in the institute at Breslau, on the effects which artificial heating of an animal exerts on the constitution of its organs, it was found that guinea-pigs, after remaining for several days in an atmosphere of 36°—38° C., displayed the most beautiful fatty changes of the liver, heart, kidneys, and voluntary muscles, while nothing whatever was observed that resembled cloudy swelling. And as regards the fatty changes, you will not forget that the exchange of gases in the blood differs greatly under these circumstances from that taking place in fever: in the guinea-pigs whose temperature was raised through the warm surrounding medium, *the absorption of oxygen and elimination of carbonic acid were diminished* (cf. vol. ii, p. 673), while in fever the production of carbonic acid is abnormally increased. If accordingly it cannot be predicted *a priori* that the accumulation of fat in the two conditions is identical, although the temperature is the same, we are no less taught by experience that the statements as to the frequent occurrence of fatty degeneration and disintegration in fever are decidedly exaggerated. In the great majority of persons dying from an acute febrile disease, even if the fever has been high, fatty gland-cells and muscle-fibres are found in no larger numbers than is common in other diseases; and though fatty heart and fatty liver are not rarely present in individuals who have suffered from prolonged, more especially hectic, fever, as the result *e.g.* of tedious suppuration or chronic tuberculosis, in this respect the febrile wasting diseases are not distinguished from the non-febrile. Everything considered, the occurrence of febrile parenchymatous degenerations cannot be reckoned among the well-established facts of pathology. Nevertheless, I do not deny that one may very possibly often succeed in drawing the conclusion from the appearances found post mortem that the individual concerned had suffered during the last period of life from severe fever. If, say, you find in a cadaver a paronychia with inflammation of the sheaths of the tendons, and in addition a fresh, soft tumefaction of the spleen, a flabby heart, and the liver and kidneys presenting an opaque, lustreless appearance, as if cooked, you may without fear of contradiction declare that the individual died with the symptoms of severe fever; yet it does not at once follow therefrom that the appearances referred to are effects and therefore signs of the fever as such. In reality, it can only be inferred from their presence that a *severe septic infection* had taken place, and it is only the experience that such infection is always accompanied by intense fever that justifies the assumption of its former presence.

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* Litten, 'Virch. A.,' lxx, p. 10.

True, the examination of the dead body, and often enough the inspection of the living, afford proof of a very different kind that the individual has suffered from a protracted and severe fever; I refer to the *emaciation*, or, as it is here more especially called, *the consumption of the body*. That such wasting must necessarily take place in every somewhat severe and prolonged fever may easily be shown. A decrease of bodily substance occurs when the physiological equilibrium between income and expenditure is disturbed so as to produce a marked augmentation of the latter. Now, we have closely concerned ourselves with the metabolism of fever patients, and were able to determine that the production both of urea and of carbonic acid is abnormally increased. Let it be clearly understood,—as compared with the normal, *i. e.* having regard to the food consumed and amount of bodily exertion undergone by the patient. The absolute amounts of urea and carbonic acid eliminated are in themselves far from enormous, and are not merely equalled but usually exceeded in health. But a healthy person producing the same amount of urea introduces a much larger quantity of albuminous substances into his body than does the fever patient, who practically partakes of no food, owing to the state of his digestive organs and the anorexia: in other words, the healthy person manufactures the urea from the albumen of the food, the fever patient in greater part at least from the albumen of the body. The excretion of urea and carbonic acid being the same in both, the body of the fever patient becomes poorer in nitrogen and carbon, while the body of the healthy individual not only undergoes no impoverishment, but may, under certain circumstances, become richer in these substances. Now it is true that an accurate knowledge of the elimination of urea and carbonic acid does not allow of our calculating exactly the changes in the weight of the body, even though the supply of albumen and fats be also taken into account; for the quantity of water present is of essential importance here. How much depends on this factor is shown, amongst other things, by the fact that in high fever the maximum weight of the body falls in the morning hours, a gradual loss taking place as the day passes; while the weight of healthy persons is least in the morning and increases till evening, owing to the food taken during the course of the day. Leyden,* who established these facts by systematically weighing fever patients, attributes the morning maximum in fever, no doubt correctly, to the larger amount of water taken during the sleepless night. He has found, further, that in no stage of a fever is the loss of weight during twenty-four hours so great as at the crisis, where he determined an average of 10·6 pro mille,—striking evidence again of the importance as regards this question of the retention and loss of water at any period. It is quite unnecessary, therefore, to refer to febrile diseases, during the course of which œdema of the skin or other form of dropsical effusion occurs, in order to make it appear intelligible that a fever patient may maintain his weight almost unreduced, despite the considerable loss of albumen and fat. Hence a single weighing during the course of a febrile disease can decide nothing; but if the patient be day after day systematically weighed, or if his weight immediately after and before the fever be compared, the loss may in the great majority of cases be certainly detected. The slight supply of nourishment is inadequate to cover the continued expenditure inseparable from life, which is moreover increased in some directions by the fever. The weight lost during a fever will depend on the elevation of the temperature, on the one hand, and the duration of the pyrexia, on the other; thus, after severe typhoid, the emaciation may be very striking, and how greatly is our pity excited by the skeleton figure of a poor phthisical patient who has suffered for months together from an uninterrupted, though not a high, fever! We are unfortunately less completely informed as to the share taken by the single organs and tissues in the febrile atrophy; for it has not yet been possible to elucidate this point by experiments such as have been carried out on continued inanition. Of course the adipose tissue, which always serves the organism as a store of superfluous material under analogous circumstances, will disappear during the febrile consumption. But it would be of greater interest to know from what parts the albumen lost by the body is taken, and this more especially it is impossible to say with certainty at present. The facts previously mentioned with regard to the subjective and objective morbid phenomena connected with the *muscular apparatus* certainly attract attention very markedly to this tissue, although I cannot recognise as just in all their details the descriptions which some writers* have given of the degeneration of the muscle-fibres during, and their regeneration after, febrile diseases. In the second place, I have already more than once stated that the increase of the pigment and potash salts in the urine indicates an augmented disintegration of *red blood-corpuscles.* In fact, Bökmann* has convinced himself by systematic counting that their number is reduced during fever, the reduction being greater the longer the fever lasts. In this way is explained the frequent presence of unusual numbers of *blood-corpuscle-containing cells* in the spleen and bone-marrow of individuals who have perished through severe febrile diseases, and I may remind you too of the instances of *hæmoglobinuria* mentioned on a former occasion (vol. iii, p. 1129) as occurring in severe fevers: for this symptom signifies simply a rapid destruction of large numbers of red blood-corpuscles, a kind of *blood-dissolution*, to which testimony is also borne in many especially pernicious cases by the occurrence of multiple hæmorrhages into the gums, muscles, pelvis of the kidney, heart, genitals, skin, &c. Yet experiences such as these again arouse the suspicion so often expressed, as to whether the consumption in febrile diseases should really be ascribed exclusively or even in greater part to the febrile rise of temperature; and it is at any rate certain that Volkmann's patients, as might be anticipated from their good appetite and scarcely disturbed digestion, underwent a much smaller loss of weight than is observed in ordinary fevers.

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* Leyden, 'D. A. f. klin. Med.,' v, p. 271.

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* Cf. Zenker, 'Ueber d. Veränderungen d. willkürl. Muskeln im Typhus Abdominalis,' Leipsig, 1864; Waldeyer, 'Virch. A.,' xxxiv, p. 473; Hoffman, ibid., xl, p. 505; 'Untersuchungen über d. pathologisch-anatomischen Veränderungen d. Organe beim Abdominaltyphus,' Leipsig, 1869.

From the foregoing remarks, you will have arrived at the conviction that we are still very far from being able to precisely define the anatomical and functional disturbances undergone by the different apparatus of the body in fever; yet despite this want, you will still regard the conclusion as justifiable that—apart from the alterations of the metabolism—the relation of those functional disturbances to the fever is simply one of dependence; all the above-described derangements of the circulation, digestion, respiration, nervous system, &c., *are, so far as they belong to the fever as such, the consequences of the febrile elevation of temperature.* Hence we were completely justified in selecting the rise of temperature as the central point of the fever. And now, having attempted to explain what we know of the causes, the pathogenesis, and the influence of fever on the functions of the individual organs of the body, it remains to briefly trace the significance of the febrile process in its bearing on the entire organism.

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* Bökmann, 'D. A. f. klin. Med.,' xxix, p. 481.

Whoever has constantly and earnestly reflected on the subject of fever will have asked himself, long before the promulgation of Darwin's doctrines,* the question,—What is the deeper significance of the process of fever, or, in clearer terms, *what advantage accrues to the organism from the febrile elevation of temperature?* The answer given by pathologists to this question has been very different in accordance with the general pathological doctrines prevailing at the time. Among the ancients the idea widely prevailed that the body rids itself of the disease or *materies morbi* by means of the fever; the importance of fever was subsequently believed to consist in its producing a change of state of the organs and juices of the body, a *retuning* of them, in a sense; and at present the most plausible conception will no doubt appear to be that the elevation of temperature is a means whereby the organism is enabled to more certainly and in particular rapidly oxidise or destroy the noxa which it is unable to directly excrete. To *prove* this assumption I readily acknowledge is impossible. Such considerations may consequently appear to you to be mere idle trifling, and certainly from a practical standpoint it is unquestionable that an estimation of the *dangers* with which fever threatens the body is of decidedly more urgent importance.

A single glance at the series of febrile functional disturbances whose main outlines I have sketched for you, suffices to show how seriously the well-being of the patients is impaired by fever. Do not fear, however, that I shall again repeat the list of morbid symptoms; we shall only concern ourselves for a moment with the features by which fever may prove directly *dangerous to life*. For if we completely disregard the local conditions by which an extensive pneumonia, a laryngeal croup, a general peritonitis or a basilar meningitis, in short so many febrile diseases, may bring about the fatal termination, there still remains a considerable number or indeed a majority of such diseases, with regard to which, as clinical and anatomical methods have increased in precision, the conviction has steadily gained ground that if they prove fatal, it is the fever that is mainly responsible. If we now seek to analyse more carefully the evil effects of fever, we find that the *consumption* due to the fever appears to present the simplest problem. For we have learned from Chossat's celebrated investigations* that the higher animals succumb irretrievably to death by starvation when, owing to deprival of food, they have lost about 40 per cent. of their body-weight. If now we assume with Leyden† that the daily consumption in fever is on the average 7 pro mille of the body-weight, a somewhat severe fever would be capable of destroying in about eight weeks an individual whose nutritive condition was moderately good, simply as the result of the continuous loss of weight. Still severer degrees of febrile wasting have, however, been observed—and that not simply in individuals who were previously very fat—without any immediate danger to life. This, it would seem, depends in some measure on the fact that after the fever has lasted long the reduction of weight becomes slighter; and it should also be considered that, just as the starving animals in Chossat's experiments were kept alive by artificial warming, so here too the febrile rise of temperature, which causes the consumption, may also be a means of prolonging the life of the emaciated individual. Everything considered, febrile consumption must not be credited with too much importance as an immediate cause of death, and least of all does it come into play in those fevers which prove fatal a few weeks or days after the commencement of the disease.

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* Cf. Leyden und Fränkel, 'Virch. A.,' lxxvi, p. 184.

In these acute cases, it is not uncommonly *the excessive increase of bodily heat* that directly terminates life. For you remember the rule derived from experience (vol. iii, p. 1330) that the life of warm-blooded animals is only compatible with temperatures which do not exceed their average heat in a healthy state by more than about 5°—6°, and that therefore a still greater increase of temperature is absolutely fatal to them. We saw the rabbits and guinea-pigs perish so soon as the limitation of heat-loss had caused a rise to 43° and 44°;

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* Chossat, 'Sur l'inanition,' 1843.

† Leyden, 'D. A. f. klin. Med.,' v, p. 271.

It is the same with the febrile increase of temperature in man. Here also a temperature of 43° or 44° leads with absolute certainty to death, which usually ensues rapidly; indeed, according to unanimous opinion of all physicians, an elevation to more than 42°, if it lasts for any time, makes a most unfavorable prognosis necessary. Yet the physician might consider himself fortunate, if none but those fever patients whose temperature rose to 42° perished. In the great majority of persons dying during and in consequence of fever, an elevation to 40·5° or at most 41° is never exceeded, and these values are often not even attained. The guinea-pigs also whose bodily heat was not raised above this point by their stay in the warm chamber were unable to bear it more than at most 5—6 days, and in fever patients it is still easier to show in what way even this temperature proves threatening to life. The effect of fever on the *heart* is in my opinion the central point of the whole. For the elevation of temperature is attended by an increased demand on the heart's work. Owing to the greater frequency of the pulse, the duration of the working phases in the unit of time is prolonged, while the periods of rest are shortened; at the same time an additional burden is thrown on the heart by the augmented activity of the respiratory muscles in fever. On the other hand, not only must the defective supply of nourishment tell most severely on those organs which have to work uninterruptedly—the respiratory muscles and above all the heart—but to this must be added the fact *that a long persistent fever regularly reduces the motive power of the heart.* Now, remember that, as the result of the consecutive fall of arterial pressure, the functions of all possible organs will suffer more or less, and that the central nervous system in particular, whose periods of recuperation have already been shortened by the sleeplessness, must have its activity impaired by the inadequate supply of arterial blood. But consider more especially what a pernicious *circulus vitiosus* arises for the heart, so soon as the coronary arteries cease to supply it with the copious stream of arterial blood which it so greatly needs precisely in fever. It must inevitably happen that its functional power, already depressed owing to the continued high temperature, will become steadily enfeebled. If the weakness of the heart is rapidly developed, a very characteristic group of symptoms may ensue, which, though no more pathognomonic of fever than are the rigors, is yet observed with extreme frequency in febrile diseases; I refer to so-called *collapse.* In the slighter degrees of collapse, the only striking symptom is the *coldness of the peripheral portions of the body,* the nose, ears, hands, feet, &c.,—a coldness which will then the more vividly contrast with the high internal temperature. A much more threatening picture is presented by the severer degrees of collapse. The patient lies pale and motionless with a feeling of the most extreme feebleness, the face is pinched, and the skin of the entire body almost as cold as ice, the sense-perceptions cease, the pulse can hardly be detected and the respiratory movements are so superficial as scarcely to be recognisable. These phenomena, it is unnecessary to explain, are all of them the direct results simply of a rapidly occurring *extreme feebleness of the heart,* in consequence of which no more blood enters the skin, the brain, the sense-organs, &c.; they are therefore, unless the cardiac weakness is rapidly overcome, the certain forerunners of death. It is only a minority of fever patients that perish with the evidences of such extreme collapse; in most, the energy of the heart is much more slowly reduced, and only very gradually declines to a degree which is no longer compatible with life. Before this point is reached, a number of days is wont to elapse, as has been emphasised more than once; and if a patient perishes during the first few days of a febrile disease without the intervention of any specially grave accident or the occurrence of an excessive rise of temperature, you may be certain that the fatal issue has been induced, not by the febrile rise of temperature as such, but by the morbid cause which originated the fever. Such deaths not uncommonly occur in cases of peracute septicæmia, occasionally in diphtheria, as well as generally in many severe infective diseases. We are accordingly again face to face with the point of so much critical importance in the entire pathology of fever, namely, that in all fevers coming under observation the disturbances of the economy of animal heat are most intimately interwoven with the other symptoms and effects of the special disease. Not till we shall have succeeded in sharply and certainly distinguishing what belongs to the particular disease and what to the morbid elevation of temperature will it be possible for us to completely understand the febrile process: then, however, I hope that the consciousness of the physician will be again imbued, but in a much higher degree, with the belief, that fever, though not free from danger, is nevertheless a "wise" contrivance of the organism.*

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* On the subject of fever, cf. the appropriate sections in the handbooks of general and special pathology and of surgery, *e. g.* Virchow, C. O. Weber, Uhle, and Wagner; also Wunderlich, 'D. Verhalten d. Eigenwärme in Krankheiten,' 2 Aufl., Leipzig, 1870; Senator, 'Untersuchungen über d. fieberhaften Process und seine Behandlung,' Berlin, 1873; Liebermeister, 'Handb. der Pathologie und Therapie des Fiebers,' Leipzig, 1875; H. C. Wood, 'Fever; a Study in Morbid and Normal Physiology,' Washington, 1880 (Smithson. Contrib.); Traube's 'Ges. Abhandlungen,' which abound in valuable information on this subject also.

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